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SUMMARY OF RECENT ABSTRACTS*

III. MALARIA†

[Continued from p. 286]

Treatment; Drug Prophylaxis; Drug Resistance

In discussing chemoprophylaxis in the indigenous people of countries where malaria is endemic, NWOKOLO (p. 8) comments that absolute immunity does not exist, and that benign attacks occur throughout life. The price of immunity is high in terms of infant and childhood mortality, and the author argues that chemoprophylaxis, with smaller doses than in Europeans, would be beneficial for the local people. He suggests proguanil, and thinks that the risk of the development of drug-resistant strains is remote. GILROY (p. 555) discusses the role of antimalarial drugs in malaria eradication and control, and points out that one of the greatest difficulties is to induce people to take them regularly.

FUHRMANN (p. 1018) describes a field test for the estimation of chloroquine in urine. In the Amazon basin of Brazil the anopheline vectors can transmit malaria in the open and are not susceptible to the action of residual insecticides; PINOTTI (p. 673) reports on the use of chloroquine in table salt, which is part of the eradication programme. HOBBS *et al.* (p. 8) report retinopathy probably resulting from prolonged treatment with chloroquine such as is used in the treatment of arthritis or lupus erythematosus. MEYLER (p. 215) reports 2 patients who developed purpura and a haemorrhagic tendency, respectively, and KALSBEEK (p. 1141) several cases of bilateral paralysis of the abducens after administration of chloroquine.

TELLO (p. 881) reports that amodiaquine has a cortisone-like action on the suprarenals, in addition to its antimalarial action. CAMPBELL (p. 1142) discusses the pigmentation which occurs in the nail-beds, palate and skin after

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1960, v. 57. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

† For previous articles on malaria in this series, see the March and April issues of the *Tropical Diseases Bulletin* each year since 1939.

prolonged amodiaquine prophylaxis; it is important to consider this before making a diagnosis of haemochromatosis or Addison's disease. The pigmentation usually disappears within 6 months after the patients stop taking the drug.

Camoprim is a preparation containing amodiaquine and primaquine; COURTNEY *et al.* (p. 784) found, in *Plasmodium vivax* malaria, that it is an effective prophylactic, and that when used after treatment of attacks with amodiaquine it could be relied upon to produce radical cure.

Having noticed that leprosy patients taking DDS experienced a feeling of wellbeing, and suspecting that this might be due in part to an effect on malaria parasites, ARCHIBALD and ROSS (p. 782) gave a single dose of DDS to schoolchildren in Northern Nigeria, and gave chloroquine to controls. They found that DDS was capable of clearing the blood of trophozoites of both *P. falciparum* and *P. malariae*, though not so quickly as chloroquine. It apparently had no effect on gametocyte or spleen rates in the doses used.

CIUCA (p. 671) shows that a single dose of pyrimethamine exerts an inhibitory action on the sporogonic cycle in *P. vivax* and *P. falciparum* infections, and this action is increased if chloroquine is also given. He suggests that a combination of these drugs as suppressives during the transmission season is an aid to eradication. AFRIDI and RAHIM (p. 673) in part of Pakistan where the transmission season is short, gave pyrimethamine on a single occasion each year before the beginning of transmission, to the inhabitants of certain villages, and found that the incidence of malaria was greatly reduced, though the infection was not completely eliminated. BRAY *et al.* (p. 337) show that administration of pyrimethamine to gametocyte carriers of *P. falciparum* was able to render them uninfective to *A. gambiae* for periods up to 28 days, and could prevent the development of pre-erythrocytic schizonts in chimpanzees treated before or shortly after infection with sporozoites. If resistance does not occur, therefore, pyrimethamine could protect man and mosquito from this infection.

It has been suggested that pyrimethamine might produce macrocytic anaemia by inhibiting the conversion of folic acid to folinic acid, and that if folic acid is given along with pyrimethamine (to reduce the risk of this anaemia) the antimalarial action of the drug might be inhibited, but HURLY (p. 100) failed to find that either folic or folinic acid interfered with the action of pyrimethamine.

CLYDE and SHUTE (p. 215) trace the development of pyrimethamine-resistant *P. falciparum* in the inhabitants of a Tanganyika village who were given weekly doses; after cessation of this treatment the incidence of fresh infections with resistant forms fell to zero in 20 months. HAINE (p. 782) from the Congo refers to the risk from weekly doses of pyrimethamine. He suggests that it should be given only in therapeutic doses during the malaria season where this is short, or in regions where control measures have reduced collective immunity. Experiments in French West Africa showed that when pyrimethamine was administered to the people twice each month, either with or without DDT spray, resistance eventually developed, and RICOSSÉ *et al.* (p. 338) also noted that therapeutic dosage did not render gametocytes uninfective to *A. gambiae*. ARCHIBALD (p. 672) attempted to eliminate malaria from a village in Northern Nigeria by giving pyrimethamine once each month, but in spite of an early reduction in *P. falciparum*, *P. malariae* and *P. ovale*, the *P. falciparum* rate reverted to its former level, indicating resistant strains, and a few trophozoites of the other two species were also found.

From Gambia HURLY (p. 101) produces evidence which suggests that sulphadiazine has a potentiating action on pyrimethamine when the two are given together.

As a result of trials in Northern Nigerian children, ARCHIBALD and ROBERTSON (p. 214) conclude that Lapudrine (a diguanide) may be a useful substitute for pyrimethamine as a single-dose treatment.

In malaria therapy work on neurosyphilitic patients with *P. falciparum* and *P. vivax* YOUNG (p. 783) found that 30 mgm. of primaquine given weekly, or 15 mgm. twice each week, or 3 or 5 mgm. daily, prevented transmission to *A. quadrimaculatus*, though gametocytes were present.

Some patients are sensitive to primaquine, and this results from a genetic defect characterized by a deficiency of glucose-6-phosphate dehydrogenase, and in those with this defect ingestion of certain drugs or foodstuffs may lead to intravascular haemolysis; BREWER *et al.* (p. 1018) describe modifications of a new test for primaquine sensitivity.

Quinocide is an 8-aminoquinoline synthesized in the U.S.S.R.; it is said to be less toxic than pamaquine, and LYSENKO (p. 1017) remarks that by reason of its success in preventing relapse, and its sporontocidal and prophylactic properties, it is suitable for clearing malarial foci in the later stages of an eradication campaign.

Control

General

In the *WHO Chronicle* (p. 216) a general account is given of the present position of the malaria eradication campaigns of the world. SINGH (p. 682) sums up the achievements and lessons of eradication campaigns, noting that resistance to insecticides has become a prominent and disquieting feature; but he thinks that in the foreseeable future the disease will cease to be a continuing health problem. FRIZZI (p. 217) comments on the achievements of the present century, when malaria has largely been eradicated in temperate countries, and on future patterns of research.

MACDONALD (p. 1020) discusses the implications of malaria eradication schemes and their planning, and mentions the importance of searching for and treating all infected persons, to remove the reservoir of infection. Malaria eradication involves total coverage and surveillance to detect remaining cases; PAMPANA (p. 681) discusses the techniques and organizations used for surveillance in 14 countries in the consolidation phase of eradication campaigns.

Malaria is mainly a rural problem, and CABRERA PALMA (p. 785) discusses the maintenance of barrier areas around towns which do not provide breeding places; these barrier areas are treated with insecticides.

YEKUTIEL (p. 1019) discusses the special problems of low-level transmission of malaria which have become evident during eradication campaigns. Conventional methods of malariometry have been found inadequate for the year-by-year assessment of the general volume of persisting malaria. Among other subjects he discusses the criteria for cessation of spraying.

RAMAKRISHNA (p. 216) reviews the role and functions of the entomologist in malaria control and eradication.

MOSNA (p. 674) recounts the great story of malaria eradication in Italy after the war during which the flooding of low-lying areas brought the disease back in rampant form; MISSIROLI directed the operations and made full use of

DDT and other insecticides, and the vectors have now gone except for a few in the south. Much progress has been made in malaria control in Rumania, and in parts spraying has been suspended, and replaced by surveillance; nevertheless DUMITRESCO *et al.* (p. 218) show that over the country as a whole the extent of spraying has been rising. RADACOVICI *et al.* (p. 785) describe the control of malaria in a river basin of Rumania.

BUSLAEV and VASYUTA (p. 675) describe the campaign against malaria in the Russian Federation Republic, where in 1958 the index fell to 0·01 per 10,000. BELIATSKY and RUBINSHTEIN (p. 11) give an account of malaria in the Bialoruss Republic since the First World War, and its control; they state that it has now been fully liquidated.

SALITERNIK (p. 102) describes 10 years of work by the Antimalarial Division of Israel; the number of new cases fell from 1,172 in 1948 to 44 in 1957. This unit is also responsible for control of culicines and of schistosomiasis.

From experience in the South Cameroons LIVADAS *et al.* (p. 218) conclude that eradication of malaria from the forest area is possible, and depends on finance.

RAO (p. 678) describes the malaria eradication programme adopted for India, which will extend over a period of 8 years; it is hoped that malaria will have been eradicated from the whole country by 1965–66. SHAMASASTRY and NARAYANA IYENGAR (p. 557) describe the organization for malaria surveillance in Mysore, where residual insecticides have been used since 1946.

Transmission of malaria in Papua and New Guinea is largely due to members of the *A. punctulatus* group, which mostly feed indoors and would be susceptible to residual insecticides; PETERS (p. 680) shows that malaria is holoendemic in some parts, and outlines a campaign which may be adopted.

Malaria has become rare in Taiwan, and surveillance is now conducted by mobile detection teams, whose work is described by CH'EN *et al.* (p. 680).

Irradiation of pupae and adults of *A. quadrimaculatus* can sterilize both sexes, and the introduction of large numbers of irradiated males into mixed communities results in reduction of fertility; DAVIS *et al.* (p. 340) suggest that this may be a possible means of control.

DE BUSTAMANTE (p. 884) discusses the difficulties of malaria eradication in Brazil, where anophelines—even of the same species—vary in their endophilic or exophilic habit in different parts of the country. DE MELLO (p. 1242) discusses the progress of the malaria eradication campaign in Brazil, with which is combined the campaign against Chagas's disease.

GOMEZ MENDOZA (p. 790) describes the procedures adopted in Mexico to evaluate the progress of malaria eradication. ALVAREZ AMÉZQUITA (p. 451) reports on the malaria campaign in Mexico, where morbidity has been reduced from 186·1 per 100,000 in 1950–54 to 21·9 in 1958, and other indices similarly. VARGAS and AMARAZ UGALDE (p. 883) show that whereas in Mexico malaria formerly accounted for some 6% of all deaths, the figure had been reduced to 1·3% by 1957.

Insecticides

Pyrethrum was formerly used with success as an antimalarial spray, and BUSVINE (p. 1241), in summing up its usage, points out that it still has a place, partly against vectors resistant to other insecticides and partly because its

effectiveness against bed bugs and house-flies would promote satisfactory public relations.

ROMERO ALVAREZ and MIRANDA FRANCO (p. 446) and FRITZ and PLETSCH (p. 446) discuss the techniques used for weighing insecticides for house spraying.

MARTINEZ-PALACIOS (p. 447) discusses the "Muralla" test for susceptibility of mosquitoes to insecticides, which is criticized in comment by Busvine, and VARGAS *et al.* (p. 883) describe a new technique for estimating susceptibility.

SUZUKI (p. 1243) suggests a method for estimating the effects of insecticides in field tests; details should be sought in the original.

COLUZZI (p. 220) investigated the irritant effect produced by contact with DDT on various anophelines; mortality records indicated that repeated contact with treated surfaces would be necessary for control of species easily irritated. He (p. 786) could not find evidence of increased resistance to DDT in anophelines tested in Italy and Sardinia.

It has been thought that a spreading agent was necessary in larvicidal oil containing DDT to overcome the various impediments to spread on natural water, but tests by MSANGI (p. 556) indicate that this is not so; wind and current help dispersion, and the insecticide itself may go into solution, or be dispersed as fine particles after the oil has evaporated.

ALKAN (p. 1021) reports on the use of DDT, dieldrin and BHC in the control of larvae in ricefields in Turkey. In general, granules and briquettes were preferred to dusts or liquid preparations.

In both treated and non-treated areas of Jordan SINGH and GAD (p. 9) failed to find evidence of resistance to DDT in *A. superpictus* larvae, but they noted that "wintering" *A. sergenti* larvae are much less susceptible than larvae found at other times of the year.

CHRISTAL (p. 12) discusses the spraying of temporary summer huts used in Northern Iraq, in which *A. sacharovi* and *A. superpictus* are found in large numbers.

MARIANI *et al.* (p. 339) show that no modification of the original sensitivity of *A. labranchiae* can be detected after 11 years of DDT spray in Sicily. ARDELEAN and CRISTESCU (p. 1143) report an increase in the period between emergence and oviposition in a laboratory colony of *A. l. atroparvus* exposed as adults in successive generations to increasing doses of DDT.

SMITH and DRAPER (p. 448) discuss the results achieved in the Taveta area of Kenya and Tanganyika after $3\frac{1}{2}$ years of spraying with dieldrin, and they find that *A. gambiae* has very largely, and *A. funestus* almost completely, disappeared. Spleen and parasite rates have fallen progressively, but *P. falciparum* may still be found in children who have never left the area, and it is possible that transmission has occurred through some unidentified secondary vector. In the third year of spraying with dieldrin in the Pare region of Tanganyika SMITH (p. 448) failed to find evidence of resistance in *A. gambiae*.

In Lower Guinea the results achieved with residual insecticides have been disappointing, largely owing to the exophilic behaviour of *A. gambiae* var. *melas*; TOUMANOFF (p. 678) suggests that permanent antilarval methods should also be used.

KUHLOW (p. 556) has investigated the effect of house spray with DDT on the behaviour of *A. funestus* in Northern Nigeria, concluding from his experiment

that these mosquitoes were repelled from entering the house; in comment Bertram suggests that the findings could be explained by other factors.

After several years of malaria control in the pilot zone of Upper Volta, French West Africa, the report in the *Cahiers de l'ORSTOM* (p. 676) shows that transmission has not been ended, but there have been changes in the patterns of behaviour of anophelines and in their importance as vectors; *A. nili* has become relatively more important. Transmission is much reduced but still continues inside houses and outside. The report analyses the situation on mathematical lines, and this approach may help towards eventual eradication, which has not yet been achieved in equatorial Africa.

A. pharoensis is a vector in several African countries, and KUHLOW (p. 786) shows that it is susceptible to DDT and dieldrin.

In part of West Pakistan where DDT has been used systematically since 1952 RAFI (p. 787) has been unable to find evidence of resistance in the local anophelines, and spleen and parasite rates show marked reduction in the sprayed areas.

NARASIMHAN *et al.* (p. 104) discuss *A. culicifacies* in Poona, where they found it highly susceptible to DDT and dieldrin. ARTHUR (p. 679) describes how virtually total control of malaria has been achieved on tea estates in Assam, largely by using BHC.

VAN DEN ASSEM (p. 449) calculated the daily mortality of 4 species of *Anopheles* in New Guinea.

BARRERA *et al.* (p. 788) have devised a method for assessing the irritation produced by DDT, in 3 Mexican anophelines, which indicated that those which have had a blood feed show much less evidence of irritation than the unfed specimens. Certain criticisms of the method are made by Busvine, in commenting on this paper.

GAHAN and HOFFMAN (p. 105) tested various insecticides against *A. quadrimaculatus*; malathion and diazinon were the most effective.

RACHOU *et al.* (pp. 11, 789) report on tests of susceptibility of *A. aquasalis* to DDT, and give details of technique; they found *A. darlingi* highly susceptible in Minas Gerais.

Resistance to Insecticides

One issue of the *WHO Weekly Epidemiological Record* for 1960 (p. 1142) contains a summary of information then available on resistance of anophelines to DDT and dieldrin. In the *Indian Journal of Malariology* (p. 218) and the report of the PAN AMERICAN HEALTH ORGANIZATION (p. 218) there are full accounts of meetings of experts to discuss the resistance of insects to insecticides, which have an obvious bearing on malaria. The records should be consulted in the originals.

MACDONALD (p. 683) discusses the genetic aspect of resistance to DDT and dieldrin in anophelines. For DDT the gene for resistance is recessive but is widely distributed; for dieldrin it is dominant but more restricted. DDT resistance takes years to become apparent but then becomes dramatic; dieldrin (and BHC) resistance arises much more rapidly. Mixtures are useful, especially in delaying the build-up of DDT-resistant populations.

ELLIOTT (p. 882) suggests that a relationship probably exists between the insecticide resistance of larvae of anophelines and adults of the same species.

De Zulueta (p. 103) discusses resistance to insecticides in *A. sacharovi*; it seems probable that there are 2 independent mechanisms of physiological resistance—one to DDT and the other to dieldrin and BHC—which may or may not be present together. Peffly (p. 104) discusses resistance to DDT and dieldrin in the anophelines of eastern Saudi Arabia.

Multiple resistance—to DDT, dieldrin and BHC—has been found by Pal Rajindar and Bhalla (p. 787) in *A. subpictus* in an area near Calcutta.

Garms (p. 1020) observed that the susceptibility of certain anopheline larvae to DDT varied according to the degree of larval development, and the stage of development is therefore an important factor in tests. Overcrowding of larvae reduced tolerance, probably as a result of partial starvation. For adults tolerance was high on emergence and after blood meals, but gradually declined with advancing age.

Frontali and Carta (p. 220) were unable to account for the resistance to DDT shown by strains of *A. l. atroparvus* on the basis of dehydrochlorination of DDT to DDE.

Darvas and Šerstnev (p. 103) show that in parts of Yugoslavia where DDT has been used for 10 years there is some degree of resistance to it in *A. maculipennis*—but not, apparently, to dieldrin and lindane. In Lebanon Shidrawi (p. 9) found no evidence of resistance to DDT in larvae of *A. superpictus*, but there was considerable difference in resistance in *A. claviger* larvae from two unsprayed villages. In Iraq, resistance to DDT was found by a WHO team (p. 9) in *A. stephensi*, but not in *A. superpictus*, *A. sacharovi* or *A. pulcherrimus*.

Maldonado-Capriles and Nasir (p. 1143) recognize DDT resistance in *A. subpictus* taken wild in the Lahore district of Pakistan. Rahman *et al.* (p. 882) found evidence to suggest the development of resistance to DDT (but not to dieldrin) in *A. culicifacies* in part of Bombay State, but in comment Busvine remarks that the findings suggest vigour tolerance rather than true resistance.

Martinez-Palacios (p. 450) reports double resistance to dieldrin and DDT in *A. quadrimaculatus* in part of Mexico where DDT is largely used for dusting cotton.

Steyn *et al.* (p. 1242) suggest a simplified gravidity technique for detecting physiological resistance of *A. gambiae* to BHC, but in comment Bertram suggests that it may allow a degree of resistance to develop undetected. Ungureanu (p. 10) used the method of topical application of alcoholic solutions of dieldrin to assess susceptibility in *A. gambiae*, and obtained results similar to those obtained with the Busvine-Nash technique for the same strains. He claims to have found a morphological difference between resistant and normal strains. Elliott (p. 9) explains that wild populations of *A. gambiae* in West Africa consist of mixtures of homozygous resistant, heterozygotes, and homozygous susceptible strains. He made an analysis of larval populations from Freetown and found dieldrin resistance (8% homozygotes and 58% heterozygotes); in Ibadan, W. Nigeria, definite resistance was not found. The capacity of insecticide-resistant anophelines to transmit malaria is not generally known, but Ramakrishna and Elliott (p. 1143) after investigating *A. gambiae* resistant to dieldrin and BHC, think that the vectorial capacity probably remains unchanged by the alteration from the heterozygous to the homozygous character.

After campaigns of spray with DDT and dieldrin in the North Cameroons *A. funestus* became rare or vanished, but MOUCHET and CAVALIE (p. 786) show that for *A. gambiae* dieldrin resistance has developed though no DDT resistance is reported.

WEINBURGH and FAY (p. 883) have established a dieldrin-resistant strain of *A. quadrimaculatus*.

In Mexico MARTINEZ PALACIOS (p. 11) reports that the selection of a strain of *A. p. pseudopunctipennis* resistant to dieldrin was accomplished within 18 weeks, but only in rice-growing areas. He found dieldrin resistance, for the first time, in *A. albimanus* in Mexico. Dieldrin resistance has appeared in anophelines of Mexico, and DDT seems to be the only practical alternative to dieldrin; BARRERA (p. 450) has found malathion disappointing in laboratory tests.

Malaria of Animals

General

HUFF (p. 682) points out that even if human malaria is eradicated many of the basic problems of malariology will still be unsolved, and the study of animal malaria will remain important.

BANO (p. 1144) studied the early nuclear division of oöcysts of several species of bird and animal plasmodia; details should be sought in the original.

Monkeys

GARNHAM (p. 1244) describes a subspecies of *P. cynomolgi* for which he proposes the name *P.c. bastianellii,* and gives his reasons for differentiating it from other subspecies. It originated in Malaya. EYLES *et al.* (p. 1244) describe several accidental or deliberate human infections in persons working with this subspecies; the infection was accompanied by marked symptoms and a low level of parasitaemia, and was easily terminated by chloroquine. They comment on the important epidemiological implications of a possible monkey reservoir of human malaria.

MAEGRAITH *et al.* (p. 340) show that in the terminal stage of *P. knowlesi* infection monkeys reach a condition of medical shock with falling blood pressure, circulatory failure and coma; noradrenaline could produce dramatic results at this stage, with quick recovery of consciousness, and additional treatment with chloroquine could even lead to freedom from parasites. The value of combating shock in such circumstances was evident, and the authors went on to study the pharmacological action of noradrenaline and similar drugs.

DEVAKUL and MAEGRAITH (p. 558) studied the phenomenon of lysis in *P. knowlesi* infection, by following the fate of red cells labelled with radioactive iron and injected into infected animals. Details should be sought in the original.

KYO (p. 1022) describes the morphology of *P. inui* as observed on phase-contrast microscopy.

ZUCKERMAN (pp. 885, 1145) studied blood loss and replacement in the malaria of monkeys, and observed that the loss exceeded that due to rupture of red cells by the parasites; this suggested that there was produced some auto-antibody to the host's own erythrocytes, altered by the presence of plasmodia.

Rodents (P. berghei; P. vinckei)

RADACOVICI *et al.* (p. 1024) have been able to transmit *P. berghei* to bird embryos. BOWMAN *et al.* (p. 1022) discuss the metabolism of *P. berghei* as observed after separation from the host red cells by means of antiserum from rabbits.

In a long series (10 years) of subinoculation experiments with *P. berghei* in white mice SERGENT and PONCET (p. 341) found that the duration of infection (to death) became shorter, and parasitaemia more severe. Exposure to chloroquine did not affect virulence, nor did passage in white rats, but resistance to chloroquine could be induced. COX (p. 221) studied relapse strains of *P. berghei* in white mice, concluding that relapses are not due to increased virulence of the parasite. In latent infections the parasites appear to produce variants which reproduce in the immune host and also give rise to relapse infections, and in new hosts these variants produce more patent infections and deaths than result from reinfection with the stock strain.

GREENBERG and KENDRICK (p. 341) noted differences in susceptibility to *P. berghei* in various hybrid strains of Swiss mice.

RILEY and DEEGAN (p. 1145) show that *P. berghei* infection of mice produces changes in the liver mitochondria, and discuss the bearing of these changes on the associated anaemia. BASU MALLIK and GANGULY (p. 13) show that the livers of rats suffering from latent *P. berghei* infection, or recovering from an acute attack, are not more vulnerable than normal livers to the toxic action of carbon tetrachloride, but that during acute attacks the livers are more susceptible. There is rapid regeneration of liver tissue after cure.

BOUISSET and RUFFIÉ (p. 684) show that whereas infected rats on normal diet resist *P. berghei*, deficiency of vitamin A is fatal to them. In experimental work on mice and *P. berghei* MACDONALD (p. 1023) has shown that a diet known to cause hepatic fibrosis increases hepatic collagen, and *P. berghei* infection also increases hepatic collagen; together these two factors cause maximal increase in collagen and produce it quickly. The excessive collagen may not remain as a permanent scar.

LAPIERRE *et al.* (p. 885) note that mice which were splenectomized and afterwards infected with *P. berghei* lived longer than infected controls; the course of infection was not influenced in mice subjected to splenectomy 7 days after infection [see also AL-DABAGH, below].

After experiments on infected white rats (involving inoculation of organ extracts into mice) COWPER and WOODWARD (p. 222) conclude that in rats with acquired resistance to infection with *P. berghei* there is a persistent latent infection of the inner organs, produced by a form of premunition, and that pyrimethamine does not entirely sterilize the cryptic infection in the organs, which is localized in the deep blood stream of the liver, spleen and heart. In a later note COWPER (p. 1144) comments that malarial pigment can be transferred mechanically to mice, and taken up by the spleen; its presence does not prove a latent infection in the donor rats, but this is suggested by bone-marrow response and the reappearance of parasites in the mice.

Various vitamins alone were found by SAUTET *et al.* (p. 223) to be ineffective in the treatment of *P. berghei* infections of mice, but B12 with chloroquine proved more effective than the drug alone in prolonging survival and preventing death.

SAUTET *et al.* (p. 222) investigated the production of drug resistance in *P. berghei* in mice; results were equivocal when small doses were given, and resistance was observed even when large doses of chloroquine were given at short intervals.

FABIANI and ORFILA (p. 1146) give an account of the pattern of infection of mice with *P. vinckei,* and note that this does not carry cross-immunity to *P. berghei.*

FABIANI *et al.* (p. 684) report that whereas adult rats resist *P. vinckei,* the infection becomes more acute if they are pregnant.

Birds

HUFF *et al.* (p. 1024) describe the techniques used in growing exo-erythrocytic stages of avian malaria parasites in porous cellulose chambers containing infected tissue, planted into various animals and chick embryos.

FERNEX (p. 685) discusses the role of mast cells in the myocardium of chickens and monkeys in experimental malaria.

SHERMAN and HULL (p. 886) report on the serum proteins in avian malaria.

TERZIAN and STAHLER (p. 791) show that differences in susceptibility of *Aedes aegypti* to *P. gallinaceum* are provoked when various inorganic acids, bases and salts are added to their diets.

RAHM and KAUFFMANN (p. 1025) investigated the effect of blockade of the reticulo-endothelial system with Indian ink, on the course of *P. gallinaceum* infection in fowls.

Antimalarial activity was found in certain guanidine derivatives when CHIN *et al.* (p. 791) tested them against *P. gallinaceum* in chickens.

DUNCAN *et al.* (p. 452) describe the electron microscope appearances of gametocytes of *P. cathemerium.*

DEMINA (p. 452) has experimented with strains of *P. relictum* which had been modified to mature at night instead of in the daytime; the original should be consulted.

TRAGER (p. 342) has detected a virus in the plasma of ducks, which interferes with the development of *P. lophurae.*

From work with *P. juxtanucleare* in chicks submitted to splenectomy either before or after infection AL-DABAGH (p. 1245) concludes that the spleen is important in acquired immunity—much more than its mere content of phagocytic cells would indicate—but is not important in relation to the initial reaction.

Lizards

LAIRD (p. 1246) describes *P. minasense* from Malayan lizards.

Charles Wilcocks

MALARIA

In this section abstracts are arranged as far as possible in the following order:—Human malaria—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control;* Animal malaria—*monkeys, other animals, birds.*

DECHIGI, M., CANALIS, A. & SEPULCRI, P. Ambiente e malaria veneti prima e dopo il D.D.T. **[Local Situation and Malaria in Veneto before and after DDT Utilization]** *Ann. de San. Pubblica.* Rome. 1960, July–Aug., v. 21, No. 4, 975–1000, 8 graphs. English summary (9 lines).

In this paper the authors deal with a territory which drains into the Adriatic Sea between the mouth of the River Po and the Gulf of Trieste. They quote the 15th Century writings of a hydraulic engineer—Marco CORNARO—to show that deficient surface or land drainage was then already seen to be connected with the incidence of fevers and ill-health. As early as 1284 there were officials responsible for land drainage and sea defences, and a Drainage Board was functioning in the Republic of Venice in 1501. The records of the Austrian Occupation Authorities refer to some 50,000 cases of malaria among the 290,370 inhabitants of this territory in 1849. Many pumping and other drainage installations have been constructed since, more especially in these last 50 years or so.

Though the indigenous species of mosquitoes are many, the main vector of malaria has been *Anopheles elutus* [*sacharovi*], which breeds in brackish waters: the critical hydrological feature for the transmission of the disease is the meeting and mixing of tidal water from the sea and fresh water from the land, and both the doctors and the engineers had realized this on empirical grounds long before the discovery of the aetiology and epidemiology of malaria as we know them now. Malaria was brought under effective control when the land was drained by pumping and tidal waters were kept out: at the same time the soil was freed from salinity and thus much improved for agriculture.

A series of legislative enactments has provided for notification of cases and for the free issue of curative and prophylactic drugs. Special dispensaries were set up to facilitate diagnosis and treatment, after-care, the care of children before and during their school years, the surveying of spleen and parasite rates, the prophylactic treatment of imported labour, the application of larvicides and insecticides and public health education.

In the 10-year period 1929–39, primary infections dropped from 5,295 to 973, and subtertian infections from 5,094 to 276. The disease caused 60 deaths in 1929, 66 in 1930 and none in 1939.

War conditions then supervened and the incidence of tertian malaria rose steadily during 1940–45, though subtertian malaria remained in abeyance. DDT became available from 1946, and until 1950 this insecticide was sprayed annually in some 37,000 homes and 164,000 animal shelters. Indigenous malaria has disappeared from this territory.

A programme of entomological and hydrological research has been carried out since 1958 and the authors stress the importance of maintaining a constant watch: any relaxation of the drainage and other agricultural operations might well restore conditions which would favour the reappearance of the disease.

J. Cauchi

SUNDER RAO, A. R., NASIRUDDIN, M., ACHUTHAN, C. & SITARAMAN, N. L. **Study of an Outbreak of Epidemic Malaria in Arasikere Taluk, Hassan District, Mysore State.** *Indian J. Malariology*. 1960, Sept., v. 14, No. 3, 253–67, 1 map & 1 folding graph.

Arasikere Taluk is about 2,650 feet above sea level and has an area of 475 square miles, with a population of about 150,000. Malarial endemicity is low, and up to 1954 no major epidemic had been reported. In that year conditions were particularly favourable for the occurrence of a regional epidemic, since after several years of deficient rainfall an unusually large amount fell in 1953, filling up all the tanks in the taluk.

From January 1954 there was a progressive rise in malaria morbidity but this was not reported until the last week in May, when the epidemic had already attained its peak. Unfortunately no observations were made in the pre-epidemic period or in the early stages of the epidemic period, but intensive studies were conducted from June 2 to 23, when DDT spraying of dwellings was begun. The peak dispensary attendance for fever was reached in the middle of May. *Plasmodium falciparum* was the chief malaria parasite concerned, but there was no obvious increase in the mortality rate, a feature ascribed to the timely intervention with drugs and insecticides. A gametocyte rate of 41·8% was recorded during the 14th to 16th weeks of the epidemic.

Mosquito densities during the epidemic were very high, the maximum prevalence of *Anopheles culicifacies* recorded being 97·0 per man-hour. A sporozoite rate of 0·4% and an anthropophilic rate of 32·5% for *A. culicifacies* were recorded.

The application of DDT spraying together with the distribution of anti-malarial drugs was followed by a marked fall in the spleen rate and mosquito densities. Infant parasite rates had fallen to zero 3 months after spraying was begun. The results are set out in great detail in 8 tables and a graph.

G. Covell

PETERS, W.; CHRISTIAN, S. H. **Studies on the Epidemiology of Malaria in New Guinea. Part IV. Unstable Highland Malaria—the Clinical Picture** [PETERS & CHRISTIAN]. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 529–36, figs. 1–3. **Part V. Unstable Highland Malaria—the Entomological Picture** [PETERS & CHRISTIAN]. *Ibid.*, 537–42. **Part VI. Unstable Highland Malaria—Analysis of Data and Possibilities for Eradication of Malaria** [PETERS]. *Ibid.*, 542–8, fig. 4. [23 refs.]

The first of this series of papers [see this *Bulletin*, 1961, v. 58, 173] gave an account of stable subcoastal malaria transmitted mainly by *Anopheles punctulatus*. The present papers are concerned with unstable highland malaria transmitted mainly by *A. farauti* at a height of approximately 5,000 feet in the Western Highlands District of New Guinea.

IV. Severe seasonal malaria epidemics commonly occur after the main rainy season. During such epidemics up to 25% of the community may be infected with plasmodia and 5% may be infective to mosquitoes. In some localities as many as 70% of the population may be infected, with a mortality rate of 1 to 2%. In the dry season parasite rates fall to about 5% and gametocyte rates to about 1%.

Plasmodium vivax is 3 to 4 times as common as *P. falciparum* and *P. malariae,* but the two last named become relatively more common during epidemics. A low degree of premunity is present in at least the older age-groups.

V. As regards entomological features the main characteristic is the variability of population density, sporozoite rate and natural longevity with the season. The peak man-biting density of *A. farauti* is 80 times its dry-season level. Sporozoite rates vary from zero to about 2%. About 70% of all *A. farauti* entering houses feed on man. This species freely enters and feeds in houses, resting on the walls after feeding.

VI. In the final paper the author presents a mathematical analysis of malaria epidemiology in the highlands of New Guinea and forecasts that eradication by residual spraying of DDT once or twice a year is a practical possibility. The optimum time for a residual spray campaign is during the first month of heavy rain following the dry season, *i.e.* November. *G. Covell*

METSELAAR, D. **Relative Increase in the Prevalence of *Plasmodium falciparum* some Years after the beginning of a House-Spraying Campaign in Netherlands New Guinea.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 523–8, 1 fig.

In 1954, house spraying with DDT at 2 gm. per sq. metre, applied at 6-month intervals, was started in the neighbourhood of Lake Sentani, in Netherlands New Guinea. Since then the area under protection has been gradually extended, with varying results. In 1958 spraying was supplemented by drug administration, a combination of 450 mgm. of a chloroquine base and 50 mgm. of pyrimethamine (adult dose) being administered 3 times at intervals of at least 1 month.

In the Sentani region, a holoendemic area, malaria incidence was considerably diminished, but transmission was by no means interrupted. The absolute parasite rate was 46% in 1953, before spraying was begun. In 1959, 5 years after the first spraying, it had fallen to 6%, but the proportion of *Plasmodium falciparum* infections had risen from 43% to 75%.

On the other hand, in the Schouten Islands, also a holoendemic area, where in most areas transmission was practically arrested by spraying alone, the proportion of *P. falciparum* infections fell from 35% in 1953 to 5% in 1959.

The author attributes these findings to the fact that in the Sentani area the proportion of infections accompanied by gametocyte production progressively increased during this period. The lessened chances which existed for *P. falciparum* to complete its extrinsic cycle in the mosquito after spraying were more than compensated for by the greater chances for the mosquito to be infected with *P. falciparum* compared with other species of parasite. The increased production of gametocytes on the part of *P. falciparum* is thought to be due to the rapid loss of immunity of the human host as soon as the number of infections is diminished. *G. Covell*

Saccà, G. Contributo alla conoscenza delle *Myzomyia* del Sud Marocchino. **[A Contribution to the Knowledge of *Myzomyia* sp. in South Morocco]** *Rendiconti Istituto Superiore di Sanità.* Rome. 1960, v. 23, Pt. 6, 575–80, 2 figs. [17 refs.] English summary (7 lines).

This paper records results of a mosquito survey in Southern Morocco during May 1959, while the author was an entomological consultant for WHO. The numbers of mosquitoes caught are given in a table showing date and place of capture. They comprise 4 species of the *Myzomyia* group: *Anopheles dthali, A. sergenti, A. hispaniola* and *A. multicolor*; and also a few *A. labranchiae*. *A. dthali,* which has wide distribution (Somalia, Ethiopia, Sudan, Egypt, Israel, Arabia, India) had not previously been recorded from Morocco.

The adult mosquitoes caught were rather few, owing to difficulties in gaining entry to traditional houses in the closely built up villages. They were caught on the shaded ground-floor rooms, not on the more open, sunny, upper rooms. The larvae were collected from pools beside the rivers. Relative abundance of the species of larvae along the course of one river is shown. At a point where *A. hispaniola* larvae greatly outnumbered *A. sergenti,* adult traps took rather more of the latter, proving its greater anthropophilism.

It is suggested that *A. dthali* may perhaps, together with *A. sergenti,* have some role in maintaining endemic malaria in the region. *J. R. Busvine*

Abul-Hab, J. K. **Observations on the Night Activities of *Anopheles sacharovi* Favre and *Anopheles superpictus* Grassi (Culicidae, Diptera) in the Sulaimaniya Liwa, North Iraqi.** *Bull. Endem. Dis.* Baghdad. 1960, July, v. 3, Nos. 3/4, 62–72, 2 graphs.

Pringle, C., Tekriti, A., Azzawi, M., Riyadh, H. & Murayati, Y. **The Anopheline Larvae of Iraq, with a Report on *A. culicifacies, A. multicolor* and *A. apoci* breeding in Syrian Desert Spring.** *Bull. Endem. Dis.* Baghdad. 1960, July, v. 3, Nos. 3/4, 36–56, 17 figs.

A brief account is given of anopheline breeding in springs along the eastern fringe of the Syrian Desert in Iraq. *Anopheles sergenti* occurs in freshwater reedy springs remote from human habitations [this *Bulletin,* 1957, v. 54, 1046], sometimes with *A. fluviatilis. A. stephensi* dominates in springs, fouled by animal pollution, in the vicinity of permanent habitations. It may be accompanied by *A. pulcherrimus,* which is also found in isolated springs with grass or *Chara. A. multicolor* was found in some highly saline springs, the first records for Iraq. Intensive breeding of *A. apoci* was in seepages from bitumen-bearing strata, water with little other aquatic life. *A. superpictus* was found once in a channel from a spring, and *A. hyrcanus* once in a heavily vegetated spring. *A. culicifacies* larvae were taken for the first time in Iraq in channels in a date garden of an oasis, but no adults were found. A revised key to larvae of these and other species is given, including *plumbeus, turkhudi, coustani* and *pharoensis* which may yet be found in Iraq. One figure illustrates the egg of *A. apoci*; the others show frontoclypeal details for different species.

D. S. Bertram

RONNEFELDT, F. *Anopheles sundaicus* (Rodenwaldt 1926) als Malariaüberträger in Mittel-Java. [*Anopheles sundaicus* **as a Vector of Malaria in Middle Java**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1959, Apr., v. 10, No. 1, 38–47, 1 fig.

The first part of this paper discusses methods of estimating the density and life expectation of anopheline mosquitoes.

The factors affecting prevalence of *Anopheles sundaicus* in Java are discussed. This mosquito breeds in brackish swamps (salinity 13 to 18 parts per 1,000 NaCl), either natural or man-made. The natural swamps are often due to silting up of the river mouths, causing brackish lagoons. These persist longest in dry seasons; heavy rain bursts the lagoon dam and temporarily destroys the breeding amenity. Man-made sites are due to the clearing of mangrove swamps and the making of fish ponds or salt evaporation pools.

Records of anopheline prevalence, based on day catches (man-hour density) or night trapping, are given for 3 places in Java, two on the south coast and one on the north coast. Some parasite indices from the same three areas are given for comparison. The significance and reliability of these data are discussed. A graph showing the anopheline density for one catching site over $4\frac{1}{2}$ years is given; it is very irregular, some of the reasons being suggested in the text. Estimates of "man-biting habit" and "critical density" as described by MACDONALD [this *Bulletin,* 1958, v. 55, 229] are calculated for the three catching sites. It is pointed out that the man-biting habit is higher on the north coast; but the prevalence of *A. sundaicus* there falls so low for 4 months that it falls below the critical density and transmission probably ceases. In contrast, the mosquito density on the south coast remains near to or above the critical density for most of the year. In general, *A. sundaicus* probably qualifies as a vector of stable malaria, despite local variations.

Control is best attempted by continual protection by house spraying (twice yearly with 0·5 gm. dieldrin per m.^{2}). Attempts to prevent siting of fish ponds near towns are likely to be unsuccessful because of local opposition.

J. R. Busvine

MARTÍNEZ PALACIOS, A. Sospechosa relación epidemiologica entre *A.* (*A.*) *apicimacula* D. & K. 1906, con un problema de paludismo. [**Suspected Relationship between** *Anopheles apicimacula* **and Malaria**] *CNEP Bol.* Mexico. 1960, July–Sept., v. 4, No. 3, 117–19.

The English summary appended to the paper is as follows:—

"It is suspected that *A. apicimacula* D. & K. 1906, might be the main vector in an area with persistence of malaria transmission. The area has been sprayed for 4 years. In spite of the fact that this anopheline has not been found naturally infected it is the most common, from those seven species in the area, and on several occasions the only one captured on human bait. This mosquito has the particular habit of biting people at their ankle."

[The area is in the north of Puebla State, Mexico.]

Martínez Palacios, A. La edad fisiológica de los anofelinos, por el método de Polovodova. [**Study of the Physiological Age of Anophelines by Polovodova's Method**] *CNEP Bol.* Mexico. 1960, Apr.–June, v. 4, No. 2, 65–73, 6 figs. on pl. [18 refs.]

The author attended the course on Advanced Entomological Techniques given to senior malariologists at the London School of Hygiene and Tropical Medicine under the auspices of the World Health Organization in 1959. This was particularly concerned with methods of determining the age of mosquitoes and the application of such data to the interpretation of epidemiological matters in malaria. The present article provides in Spanish, and with illustrations, an account of the technique and its use, and contributes some results obtained for Mexican species of *Anopheles*.

In the first half of March 1960, dissections of *Anopheles albimanus* [numbers?] showed 34% nulliparous, 61% uniparous, 4·5% biparous, and none with three or more ovipositions completed. Since a complete oviposition cycle required probably 3 days, the mosquitoes were not at that time living long enough (13 days) to transmit malaria. [The author follows the Russian concept that a "gonotrophic cycle" consists of 3 phases: (1) finding and feeding on a host, (2) digestion of the meal and maturation of eggs and (3) selecting a breeding place finally for oviposition.] [See also this *Bulletin*, 1958, v. 55, 713.]

D. S. Bertram

Al-Dabagh, M. A. **Mechanisms of Death and Tissue Injury in Malaria. VI. Malarial Toxins.** *J. Facul. of Med., Baghdad.* 1960, Oct., v. 2 (n.s.), No. 4, 135–40. [28 refs.]

"The production of a toxin by the malarial parasite has been postulated by several workers; but such a toxin has not, as yet, been demonstrated as being secreted or produced by any malarial parasite."

Clyde, D. F. **Tasteless Chloroquine Preparations.** *East African Med. J.* 1960, Aug., v. 37, No. 8, 543–9.

A trial of disguised or tasteless preparations of chloroquine, both for their acceptability and for their therapeutic effectiveness, was made among infants and toddlers of all races in Tanganyika. Hyperendemic malaria, mainly subtertian, is present in the area. Methods to disguise the bitter taste of chloroquine salts were first tried. Chloroquine sulphate syrup and chloroquine phosphate elixir were not very acceptable, small children disliking the elixir particularly. The antimalarial activity was the same as that of the corresponding salts. Enteric coated pills each containing 75 mgm. chloroquine base were similar in size to an ordinary phosphate tablet of 150 mgm. base. The pills were very hard and were readily swallowed by older children, but were too large for infants and toddlers. The antimalarial activity was almost equal to that of standard preparations though there was some evidence of inadequate absorption of the chloroquine in 2 patients. Sugar-coated preparations in the form of pinhead-sized granules had a hard outer coat of sugar. Half a gramme

(about 95 granules) made up a dose of 75 mgm. chloroquine base. The dose was given on jam or honey, in most cases without difficulty. The antimalarial action was equivalent to that of an equal dose of the standard preparations.

Two tasteless salts of chloroquine were tried. Chloroquine methylene-hydroxynaphthoate in 75 mgm. tablets was tasteless or slightly yeasty. Its action was capricious, and only a dose which was 7 times the successful phosphate dose was always effective. Therefore its use was abandoned. Chloroquine tannate was supplied in tablets and as a flavoured liquid suspension. The tablets, 75 mgm. base, were of the size of chloroquine phosphate tablets having 150 mgm. base. The large size of the tablet was thus, again, a disadvantage for small children, and also it was only half as effective as the same amount of phosphate. Fluid suspensions, flavoured with orange or chocolate, were successful in concealing the slight taste of the chloroquine tannate but the Bantu mothers believe that all antimalarials should taste like quinine and so all did not permit their children to sample the flavoured suspension. For clearance of parasitaemia a dose of tannate double that of phosphate was required, and even then there was one failure among 83 infected children who were treated.

Absorption of chloroquine hydroxynaphthoate was shown to be impaired if it was given with an antacid [CLYDE and SHUTE, this *Bulletin*, 1958, v. 55, 982] but this compound modified with hydrochloride proved very effective though it was very bitter. Excretion of chloroquine in the urine may be determined by using methyl orange [HASKINS, *ibid.*, 980] and trials reported in the paper show that antacid given with chloroquine tannate apparently does not impair its absorption, whereas absorption of hydroxynaphthoate is impaired when antacid is given with it. *S. Bell*

SANDHINAND, U. **The Use of "Lapaquin" in Single Dose Treatment of Malaria.** *J. Trop. Med. & Hyg.* 1960, Nov., v. 63, No. 11, 266–9, 1 map.

Lapaquin, a recently introduced antimalarial developed by Imperial Chemical Industries, is a compound containing in each tablet 150 mgm. chloroquine base with 20 mgm. of chloroguanil, a new proguanil derivative.

The drug has been used in an attempt to obtain parasite control in a hyperendemic malarial zone bordering forested hills in the Eastern Coast region of Thailand. In this area the villages are too remote and inaccessible to permit the use of residual insecticide sprays. Each house was visited and blood films were taken from every person who had suffered an attack of fever during the previous 7 days. Those adults who showed parasitaemia were treated with 4 tablets of Lapaquin as a single dose. Adolescents of 10–15 years received 3 tablets, children of 6–9 years 2 tablets, those of 1–5 years 1 tablet and infants ½ tablet. *Plasmodium vivax* and *P. falciparum* were the only species identified. Eight rounds of visits were made between August 1958 and October 1959 and 1,238 persons were treated out of a local population of 19,376.

A parasite count per 100 leucocytes was made before treatment and was repeated 24 and 48 hours after drug administration. Asexual parasites were eliminated within 48 hours in all but 1 patient, a boy of 3 years with an intense *P. falciparum* infection, in whom scanty parasites persisted. Though

gametocytes of *P. vivax* disappeared completely, those of *P. falciparum* were not reduced during the observation period. No serious side effects of the drug were noted.

All habitations in the experimental area were revisited at regular intervals and records were made of all those treated patients in whom blood parasites reappeared. [Whether these represented relapses, recrudescences or reinfections is entirely conjectural.] In general, the incidence of recurrent parasitaemia was very low, about 1%, though it was relatively higher in children who had received only 2 tablets than in those to whom the full adult dose of 4 tablets had been given. 2 tablets may represent too small a dose.

[Lapaquin in this dosage appears effectively to eliminate asexual parasites in the population examined, who may be presumed to have acquired a degree of premunity. Much more detailed study is required, however, in order to establish its full therapeutic potentiality in human malaria.] *J. H. Walters*

BASAVARAJ, H. R. **Observations on the Treatment of 678 Malaria Cases with Primaquine in an Area Free from Malaria Transmission in Mysore State, India.** *Indian J. Malariology*. 1960, Sept., v. 14, No. 3, 269–81, 1 map.

Malaria in this area was hyperendemic before 1949. Spraying of houses with residual insecticides was begun in 1948, resulting in an immediate steep fall in malaria morbidity, followed by a further reduction in transmission to a point where the incidence of fresh cases was restricted to the immigrant labour force employed on the Bhadra Reservoir Project.

During the period November 1957 to July 1959, 2,314 fever patients were treated with a single dose of 0·6 gm. of camoquin, followed by a course of 15 mgm. of primaquine base daily for 5 days. No toxic symptoms were observed from this regimen. Blood smears taken before treatment were found positive for malaria parasites in 678 cases (*Plasmodium vivax* 563, *P. falciparum* 110, *P. malariae* 1, mixed infections 4). The relapse rate in this group was 5·75%, whereas in another group of 47 patients treated over a period of 10 months with a single dose of camoquin the relapse rate was 40%.

G. Covell

GAUDETTE, L. E. & COATNEY, G. R. **Stability of Primaquine Diphosphate under Various Conditions.** *Amer. J. Trop. Med. & Hyg.* 1960, Sept., v. 9, No. 5, 532–5, 1 fig.

It is known that suppression of malaria can be obtained by adding appropriate amounts of antimalarial drugs such as chloroquine and pyrimethamine to the salt used in the diet [this *Bulletin*, 1959, v. 56, 122]. In the present experiments, an investigation was made to see if primaquine was sufficiently stable under conditions of cooking to be used in the same way.

Primaquine was 95% stable to heating in oil to 100°C. for 24 hours, 70% stable to dry heat 100°C. for 24 hours, 47% stable to boiling water for 24 hours but only 6% stable to 200°C. in oil for 1 hour. In the last case the compound changed into tar-like material. When the various samples were tested on chicks infected with *Plasmodium gallinaceum*, all the heated samples

had lost their antimalarial activity except the sample boiled in water for 24 hours, and this retained only a low activity. It is concluded that primaquine is not suitable to be added to salt as part of a malaria eradication programme.

F. Hawking

ARCHER, T. C. R. **A Note on the Use of Daraprim as a Malaria Prophylactic in Nigerian Troops and their Families.** *J. Roy. Army Med. Corps.* 1960, Oct., v. 106, No. 4, 182–5.

The personnel of a Nigerian infantry battalion stationed in Eastern Nigeria, together with their families, were given Daraprim (pyrimethamine) as a prophylactic against malaria in a dosage of 25 mgm. every 14 days from November 1957 to June 1958, and 25 mgm. every 7 days from July 1958 to March 1959, children under 7 years of age receiving half that dose.

Figures are given in tabular form showing the monthly malaria attack rate in the treated battalion A and in 2 other battalions B and C living in other stations under comparable conditions, who received no antimalaria drug.

In October 1957 the monthly attack rate per 1,000 was 21 for Battalion A, 55 for B and 29 for C. The average monthly attack rate after the commencement of Daraprim prophylaxis was 3·4 in Battalion A, 35 in B and 58 in C.

There was thus a very striking reduction in malaria incidence in Battalion A as the result of Daraprim prophylaxis. Malaria has virtually disappeared among the troops and has been greatly reduced among the families. The higher rate among the families is attributed to the fact that the soldier consumes his tablet on parade, while it is not practicable to parade the family.

G. Covell

CLYDE, D. F. **Prolonged Malaria Prophylaxis through Pyrimethamine in Mothers' Milk.** *East African Med. J.* 1960, Oct., v. 37, No. 10, 659–60.

The author and his colleagues have already shown that adequate quantities of pyrimethamine given to lactating Bondei women in Muheza, Tanganyika, were excreted in the milk and had an antimalarial activity in the babies, but the method cannot be relied upon in Bantu infants because of variations in feeding before weaning [this *Bulletin,* 1957, v. 54, 1154]. In these cases the dosage in the mothers was 70 or 50 mgm. and malaria parasites disappeared from the blood of all babies concerned who were predominantly breast-fed. It was thought that if the mother took only 25 mgm. of pyrimethamine weekly, this would be barely sufficient to prevent parasitaemia in the infant. The quantity taken by the baby as a result of 25 mgm. doses in the mother was shown to be 3·4 to 4·5 mgm. between 4 and 8 months, an amount just sufficient to protect the infant if milk flow, feeding and absorption were not impaired: the amounts required by infants for effective protection has, in fact, been shown to vary from 1·7–3·4 mgm. to 2·2–4·3 mgm. between 4 and 8 months [*ibid.,* 1952, v. 49, 663].

In the previous work the maternal dose had been greater than 25 mgm. weekly and the longest period of prophylaxis was 2 months: also, resistant strains of *Plasmodium falciparum* were present in the area. The author now

records the case of a Bondei woman in a holoendemic area who took her infant aged 4 months to a local Mission clinic with severe proved subtertian malaria. After the baby had been treated, the mother was given 75 mgm. pyrimethamine and thereafter received 25 mgm. weekly for 6 months in the presence of the Sister. The baby remained healthy, free of malaria and gained weight rapidly.

When the baby was 10 months old, the Mission Sister fell ill and the mother missed 2 consecutive weeks of treatment: in the third week the baby was found to be suffering from subtertian malaria with heavy parasitaemia.

No mosquito nets or other personal protection had been used. Unprotected infants in the area have a parasite rate of 85–90%. There is thus no doubt that the maternal treatment was an effective prophylaxis for the 6 months in which the drug was passed in the mother's milk. *H. J. O'D. Burke-Gaffney*

CLYDE, D. F. **Cross-Resistance of Malaria Parasites.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 597–8.

In a mass chemoprophylaxis project undertaken at Mkuzi, Tanganyika [this *Bulletin*, 1958, v. 55, 733], daily treatment with proguanil of pyrimethamine-resistant *Plasmodium falciparum* resulted in clearance of asexual forms. This apparent lack of cross-resistance is at variance with observations reported from elsewhere.

Now, 3 years later, the author finds that in the same area 20% of asexual *P. falciparum* parasites fail to be cleared by 25 mgm. pyrimethamine and of these half do not respond to 75 mgm. In May and June 1960, proguanil and Lapudrine (dichlorophenyl-isopropyl diguanide) were administered for 6 weeks to children aged 6–10 years and blood examinations were made 7 days after the last dose.

The results showed the presence of cross-resistance between pyrimethamine and the 2 biguanide drugs, thus refuting the observations made in 1957. The only explanation offered is that the cross-testing doses of proguanil given in 1957 were greater than those given in the present investigation. *G. Covell*

MÁRQUEZ ESCOBEDO, M. B. Estado actual de la erradicación del paludismo en México. [**Present Position of Malaria Eradication in Mexico**] *Bol. Oficina Sanitaria Panamericana.* 1960, Nov., v. 49, No. 5, 414–23, 7 figs.

See also this *Bulletin*, 1961, v. 58, 13.

GUARITA, O. F. & LIMA, A. R. Suscetibilidade do *Anopheles* (*Kerteszia*) *cruzii cruzii*, ao DDT. [**Susceptibility of *Anopheles cruzii* to DDT**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1960, Sept., v. 25, No. 85, 185–7, 1 graph. English summary.

This anopheline, from the Cananéia area, São Paulo, was highly susceptible to DDT.

HECHT, O., CHAPA SALDAÑA, H. & HERNANDEZ CORZO, J. La influencia de la luz en las reacciones de huída de los mosquitos anofelinos irritados por el contacto con DDT. **[Influence of Light on the Flight Reactions of Anophelines irritated by DDT]** *CNEP Bol.* Mexico. 1960, July–Sept., v. 4, No. 3, 129–46, 1 fig. & 6 graphs. [20 refs.] English summary.

The authors continue their studies on the irritant effect of DDT on mosquitoes [see BARRERA *et al.*, this *Bulletin,* 1960, v. 57, 788 and HECHT and HERNANDEZ CORZO, *ibid.*, 1961, v. 58, 294]. In this paper a slightly different apparatus is used. It consists of a 50 cm. cubic box, from one side of which a rectangular tunnel projects (20 cm. × 20 cm. × 150 cm.). The box is lined with filter paper, which can be replaced with paper impregnated with DDT (0·5 gm./m.²). The box and the tunnel can be illuminated to different degrees. Mosquitoes put into the box can escape into the tunnel, but cannot easily return, because of a funnel device.

The degree of excito-repellent effect was investigated with groups of the following mosquitoes: *Anopheles aztecus* (azt.), *A. quadrimaculatus* (quad.) and *A. albimanus* (alb.) under the following degrees of illumination: daylight (L), artificial light (AL), semi-darkness (S) and darkness (D). The following table shows the percentages of mosquitoes which escaped into the tunnel after 1 hour.

Box	Tunnel	Unfed			Blood-fed		
		azt.	*quad.*	*alb.*	*azt.*	*quad.*	*alb.*
L	D	100	100	70	98	50	75
L	L	35	5	80	23	0	37
S	S	37	12	37	43	5	2
D	S	17	0	20	10	5	0
AL	S	100	78	48	98	85	45
D	D	43	10	23	48	15	18

The following conclusions may be drawn. (1) Blood-fed mosquitoes behave roughly in the same way as those unfed, but are less active. (2) The order of decreasing response to excito-repellent effect is azt.>alb.>quad. (3) The biggest migration occurs from a lighted box to a dark tunnel. There is less activity when both are equally illuminated and least when the tunnel is lighter than the box. [Thus the DDT-irritated mosquitoes seem to avoid light, in contrast to the observations of KENNEDY (*ibid.*, 1947, v. 44, 561), and TRAPIDO (*ibid.*, 1953, v. 50, 192), who noted that DDT-irritated mosquitoes were attracted by light.]

Similar experiments were done without DDT-treated paper, as a control. Movement to the tunnel was slight except for the condition where the box was "AL" and the tunnel "S," when migration sometimes reached 30–40%.

J. R. Busvine

YOELI, M. & MOST, H. **The Biology of a Newly Isolated Strain of *Plasmodium berghei* in a Rodent Host and in Experimental Mosquito Vectors.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 549–55, 28 coloured figs. on 2 pls. [11 refs.]

Two successful attempts to infect laboratory-bred mosquitoes with *Plasmodium berghei* have previously been reported [this *Bulletin,* 1952, v. 49, 932; 1954, v. 51, 467] but when the procedures were repeated by other workers negative results were invariably obtained.

The present work is a report on 3 successive cyclic transmissions of the *Plasmodium* in *Anopheles quadrimaculatus,* in *A. aztecus* and in the young white rat host. A strain of *P. berghei* recently isolated in the former Belgian Congo from salivary glands of *Anopheles dureni* was sent to the authors' laboratory in New York in white mice and hamsters. The strain was named Kasapa SP 7307 and it gave rise to many gametocytes. Three strains, NYU (New York University) 1, 2 and 3, were subsequently isolated by the method indicated above. The methods of maintaining the two species of mosquito are described, and there was a high mortality with *A. aztecus.*

A. quadrimaculatus were fed on 3 successive days on infected hamsters and maintained at 26–27°C. The course of infection in the mosquito was followed by dissection and the use of histological techniques. Sporozoite-induced infections were then obtained in white rats 15–20 days old from the same litter in separate experiments by means of intraperitoneal inoculation (once by intravenous injection) and the prepatent period varied from 3 to 10 days.

Attention is drawn to some morphological characters of *P. berghei* not previously described. Oökinetes were abundant in the stomachs of the 2 species of mosquito 20–24 hours after feeding and made experimental work easier. A detailed study of oöcyst development was made in both mosquitoes in which the infection rate was in each case about 90%. Sporozoite formation was also studied.

The authors point out that the animals used were litter mates, the mosquitoes were from one batch and techniques standard so that failure to obtain infection in all animals suggests that viability of sporozoites is all-important.

Parasites appearing in the blood at the earliest times are described in detail and also the different developmental stages of the sporogonic cycle. There are also some excellent coloured illustrations, all of which are worth study in the original. *J. D. Fulton*

TRYPANOSOMIASIS

*In this section abstracts are arranged as far as possible in the following order:—*African*—human, animal;* American*—Chagas's disease and other trypanosome infections. In each form the following order is followed:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.*

MORRIS, K. R. S. **Studies on the Epidemiology of Sleeping Sickness in East Africa. V. Sleeping Sickness in the Bunyoro District of Uganda.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 585–96, 1 map. [12 refs.]

This paper is mainly of historical and local interest. The Bunyoro District of Western Uganda is bounded by Lake Albert on the west and by the Victoria Nile on the north and east. A fairly severe epidemic of Gambian sleeping sickness was, by 1905, already established in a focus on the north-east side of the lake, whence the disease spread southwards down the eastern shore. The removal of the population, 1909–10, from the *Glossina palpalis* infested banks of the lake shore, its tributaries, and from the Victoria Nile, resulted in a striking and progressive reduction in the number of deaths, but led to the surrender of great tracts of country to *G. morsitans* and *G. pallidipes*. From 1920 to 1923 the people were resettled along the lake shore, and although there is little information available for the period 1925–40, it would appear that sleeping sickness was rare in Bunyoro District. From 1940 to the present day the disease has been introduced from epidemic sources outside Bunyoro by the stream of migrant labourers entering from the north; several cases have occurred on the shores of Lake Albert, but considerably more on the eastern side of the district on the Victoria Nile and its tributaries.

In 1941 an epidemic of the Rhodesian form of the disease developed to the south in Southern Busoga; its threat to Bunyoro District was successfully met by the establishment of inspection posts on the main points of entry used by returning labourers; however, in 1948, one such labourer was responsible for starting a small outbreak in south-east Bunyoro which was at once stamped on; by 1954, both *G. morsitans* and *G. pallidipes* had been eradicated from this danger point [see also this *Bulletin*, 1960, v. 57, 106, 562].

T. A. M. Nash

WESTPHAL, A. Reflexmikroskopische Untersuchungen am Kern und Blepharoplast einiger Trypanosomen mit dem Azureosin-Reflektor (Giemsafärbung). **[Reflex-microscopic Studies on the Nucleus and Kinetoplast of Trypanosomes with Azure-Eosin Reflector (Giemsa Stain)]** *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1960, v. 11, No. 1, 24–35, 9 figs.

Owing to limited resolution of the conventional light microscope, the minute cellular structures of the object examined are not clearly visible. However, the author has developed a method of reflex-microscopy (to be fully described in a forthcoming publication), whereby the object is illuminated from above with a top illumination condenser, as used in metallurgy, and viewed through an oil immersion objective. Any part of the object which reflects light will therefore form an image.

The author has used this method for the study of the cytology of trypanosomes stained by the Giemsa method, in which azure-eosin acts as a reflector, thereby revealing those constituents of the flagellates that are coloured with this dye. A comparison is made of the inner structure of the same individual trypanosomes (*Trypanosoma cruzi, T. lewisi, T. gambiense* and other members of the *brucei* group) examined successively by conventional and reflex-microscopy, and illustrated by photomicrographs.

The reflex microscope reveals the flagellum as a yellow-green filament which —contrary to the accepted view—is never free but is encased in an extension of the pellicle [=flagellar sheath?] throughout its length. The colour of the cytoplasm varies, according to the physiological state of the flagellate, from brown, red, orange or yellow. The nucleus and kinetoplast in non-dividing trypanosomes emit a metallic green light and appear to be larger than with ordinary illumination, whereas in those trypanosomes which multiply continuously in the blood (*brucei* group) these organoids appear to be devoid of colour, but their cytoplasm contains numerous reflecting granules. On the other hand, in non-dividing *T. gambiense* from a human case of infection the coloured substance was concentrated only in the nuclei and kinetoplasts. The volutin granules present in the cytoplasm produced the same colour reaction as the last-named organoids.

It is suggested that the substance revealed by reflex-microscopy in the nucleus and kinetoplast, which may be released into the cytoplasm, might represent RNA, while the similarity of the reaction of these two organoids supports the view that the kinetoplast has a metabolic function. *C. A. Hoare*

Inoki, S., Nakabayashi, T., Fukukita, S. & Osaki, H. **Studies on the Immunological Variation in** *Trypanosoma gambiense*. **IV. Further Considerations on the Screening Method.** *Biken's J.* Osaka. 1959, Dec., v. 2, No. 4, 277–83, 1 fig. [12 refs.]

This paper is concerned with technical details in the study of immunological variation of *Trypanosoma gambiense* produced when mice that have been infected with this organism are treated with human serum [Inoki *et al.*, this *Bulletin*, 1958, v. 55, 486.] Since these results are standardized in terms of volumes of "officinal" [?stock] human serum, the results are only of interest in considering other parts of this particular study; they are not of general application. *W. E. Ormerod*

Lapierre, J., Rousset, J. J. & Picot, H. Réceptivité du hérisson (*Erinaceus europaeus*) au *Trypanosoma gambiense*. [**Susceptibility of the Hedgehog to Infection with** *Trypanosoma gambiense*] *Ann. Parasit. Humaine et Comparée*. 1960, v. 35, Nos. 1/2, 188–9.

9 hedgehogs (*Erinaceus europaeus*) were inoculated by different routes with variable numbers of a virulent strain of *Trypanosoma gambiense*. In 8 cases the resulting infection was acute, killing the animals in 5–12 days. In one case the course was chronic, killing the animal after 41 days, but this hedgehog had a concomitant infection with *Borrelia* [*Spirochaeta*] *crocidurae*. *C. A. Hoare*

CHAPMAN, R. F. **A Note on *Glossina medicorum* Aust. (Diptera) in Ghana.** *Bull. Entom. Res.* 1960, Nov., v. 51, Pt. 3, 435–40, 2 text figs. & 2 figs. on pl.

A vehicle moving through bush at about 5 m.p.h. was a useful method of catching *Glossina medicorum,* otherwise not readily obtained in Ghana, as well as *G. palpalis* and *G. longipalpis*. Near Accra, *G. medicorum* occurred in thicket not more than 15 ft. high, interspersed with grass clearings, and also in secondary thicket from Takoradi east towards the Volta River. In the area north of Accra, bush-buck may have been its food host but other possible hosts present in the area are listed. This fly was most active about sunrise, most numerous in April and October, and showed considerable size variation from time to time. Small flies appear to result from dry atmospheric conditions during their pupal life and some part of the life of the parent flies—a period of about 2 months. *D. S. Bertram*

BURSELL, E. **The Effect of Temperature on the Consumption of Fat during Pupal Development in *Glossina*.** *Bull. Entom. Res.* 1960, Nov., v. 51, Pt. 3, 583–98, 5 figs. [22 refs.]

The tsetse larva when deposited by the female fly contains large quantities of fat which are the sole source of its energy during the pupal period and for the emerged fly before its first blood meal. Experiments, mainly with *Glossina morsitans,* show that the least amount of fat is consumed in pupae kept at 22° and 24°C. At higher temperatures the fat is more rapidly used up but without a corresponding shortening of the pupal period. At low temperatures the pupal period is greatly lengthened but fat consumption still continues at a considerable rate tending to exhaust fat reserves before emergence.

It appears, then, that mortality due to exhaustion of fat reserves at both high and low temperatures during pupal life may be an important factor in limiting the numbers and distribution of flies; a tendency towards selection of larger individuals seems also likely to result, as larger puparia have more fat reserve. Such implications are discussed in relation to findings in the field for several tsetse species. The lower limit for the processes of pupal development is probably 4°C., but it is thought likely that, at such low temperature, fat reserves would be exhausted before final completion of development.

D. S. Bertram

MORRIS, K. R. S. **Trapping as a means of studying the Game Tsetse *Glossina pallidipes* Aust.** *Bull. Entom. Res.* 1960, Nov., v. 51, Pt. 3, 533–57, 2 text figs. & 4 figs. on pl. [13 refs.]

Glossina pallidipes is not readily caught by fly-boy rounds and its presence may remain undetected by such conventional methods. Bait-ox, or a screen, have long been considered essential to survey for this species, which is important widely as a vector of cattle trypanosomiasis in East Africa and, since 1940, of human Rhodesian sleeping sickness in Uganda and Kenya

along the northern shore of Lake Victoria. This paper discusses at length trials in Uganda of traps (these are illustrated) for *G. pallidipes,* based on the design and principles of the Harris-type baitless trap used by the author for *G. longipalpis* in West Africa in 1949 [this *Bulletin,* 1949, v. 46, 618]. Various modifications of size and colour were tried—black being notably successful, two traps of this colour catching 2,312 flies (in 14 months' trial) of which 82·3% were females. The traps were better than boys on fly rounds, not only in catching larger numbers but more females and, in fact, giving generally a more representative sample than conventional fly rounds. The traps caught 5–15 times more flies than screens on cycling fly-boys.

These preliminaries having been established, trapping was instituted to study *G. pallidipes* in a fly-belt 1 mile east of, and also in, Busakira Settlement, an illegal squatters' settlement in the bush infected with *Trypanosoma rhodesiense,* about 25 miles east of Jinja, Uganda. Traps were variously sited (diagram given) in open grass and in or near thicket and paths, and in forest. The true habitat where numbers were greatest is shown to be the narrow zone of broken thicket between forest and open grassland. Closed canopy forest was not occupied but a secondary habitat is regenerating forest with broken canopy. Catches in traps were highest from 10 a.m. to 4 p.m. Migrant elephant herds were shown to introduce large numbers of new fly to the area—swarms of up to 307 fly (84% female). This was not certainly so with buffalo, increased fly catches being explicable simply by fly concentration on the buffaloes.

In the work in the settlement itself, there was a notable reduction of fly for the first 2 months of trapping followed by persisting low catches. This is interpreted as "catching out" effect on a resident fly population with, subsequently, infiltration of small numbers from the fly belt outside the settlement. In general, too, fly numbers were clearly less in the settlement despite its proximity to the fly belt.

These studies have already been put in practice in reclaiming land from the tsetse belt in the South Busoga Resettlement Scheme which aims to develop, by compact settlement, land for years prohibited by law to man on account of transmission of Rhodesian sleeping sickness by *G. pallidipes.* A fuller account is to follow. *D. S. Bertram*

WEINMAN, D. **Cultivation of the African Sleeping Sickness Trypanosomes from the Blood and Cerebrospinal Fluid of Patients and Suspects.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Mar., v. 54, No. 2, 180–90. [26 refs.]

A description is given of a new method for cultivation of *Trypanosoma gambiense* and *T. rhodesiense,* under African conditions, for use in the diagnosis of sleeping sickness. The medium consists of two portions: (a) base composed of 1·5% Difco nutrient agar (at *p*H 7·3) 31 gm., plain agar 5 gm. and distilled water 1,000 ml.: the ingredients are dissolved by heating, distributed in known volumes and autoclaved; (b) inactivated human plasma and washed human erythrocytes at 200 ml. each. Before use, blood is reconstituted by mixing equal volumes of the plasma and erythrocytes, then 3 times as much base (a) is cooled to 45°C. and 1 part of reconstituted blood (at same temperature) is added to 3 parts of base (a). The resulting medium is

distributed in test tubes (5 ml. each), these are slanted (2–3 days), and—after incubation to test sterility—stored at 4–8°C.

To each ml. of blood used for cultivation is added 0·1 ml. of 0·5% saline solution of anticoagulant PVSA (polyvinyl sulphuric acid) sterilized by filtration, and 2 ml. of blood + PVSA are inoculated into each tube of medium, to which dihydrostreptomycin sulphate (0·5 mgm. in 0·1 ml. saline per 1 ml. blood) has been added; the inoculum is spread over the surface of the medium by tilting the tubes, and these are incubated at 25°C. in darkness. The cultures may become positive between 5 and 30 days.

In trials carried out in East Africa, blood was cultivated from 155 persons, comprising patients, in whom the parasitological diagnosis was made by standard methods, and suspects. Of the 34 patients, 27 (79%) gave positive blood cultures, while in the 7 remaining cases the cultures were contaminated. Among 22 suspects, positive cultures were obtained in 5 (23%). Positive results were also obtained in cultures of the cerebrospinal fluid. In about 20% of the cultures the parasite was *T. rhodesiense*, in the rest *T. gambiense*.

The culture method described proved to be sensitive and reliable, providing —in the author's words—" An independent means for estimating the accuracy of conventional diagnostic methods " in sleeping sickness. *C. A. Hoare*

PAYET, M. & SANKALE, M. Hyperazotémies transitoires consécutives au traitement de la trypanosomiase humaine africaine par les diamidines. [**Transitory Hyperazotaemia after Treatment of African Trypanosomiasis in Man with Diamidines**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 690–96.

4 patients with African trypanosomiasis were treated in West Africa with Lomidine (the dimethanesulphonate of diamidinodiphenoxy pentane). One of these was a European, the others were African. All 4 patients developed a transitory hyperazotaemia during treatment with the drug, one of them with no resultant subjective symptoms, one with severe symptoms in the form of vomiting, loss of visual acuity and semi-coma, and the other 2 with anorexia, nausea and lassitude only. The blood urea levels in all 4 were found to be high, but their urines remained free from albumin, casts and blood and their arterial blood pressures did not rise significantly. The blood urea levels were repeatedly estimated throughout and after the end of treatment in 2 patients; these levels returned to normal within 2 or 3 weeks of the completion of Lomidine treatment.

The authors ascribe the hyperazotaemia to the chemotherapy and they believe that it is a much more constant accompaniment of diamidine treatment than has hitherto been appreciated; it has not been detected because it develops insidiously and it has not been specifically sought for. Its clinical manifestations are hypersalivation, anorexia, nausea and sometimes vomiting; though these often are not pronounced they may be violent and be associated with visual defects and semiconsciousness; such symptoms are often encountered during Lomidine treatment and their origin now becomes clear. In the authors' hands the dosage of Lomidine given was conservative (2 mgm./kgm. of body weight initially, rising through 3 to 4 mgm./kgm. by the third

injection and the latter repeated on another 4 occasions, all at 2-day intervals). The spontaneous disappearance of the reaction without permanent defect indicates that the use of Lomidine can be continued for the treatment and prophylaxis of trypanosomiasis as hitherto. The mechanism causative of the hyperazotaemia is not clear; it has been encountered in healthy controls and so cannot be associated with the fever, the parasitic infection or trypanolysis caused by the drug. Attachment of the aromatic diamidine drugs to the kidneys and suprarenals may possibly account for it, and renal biopsy may throw light on this possibility.

In comment J. SCHNEIDER thought that the hyperazotaemia could not be of renal origin in view of its lack of association with urinary changes and the rapid recovery from it. He discussed the changes which are known to occur in the balance of the blood globulins in parasitic infections of man, and their possible bearing on the matter. He did not think that kidney damage by attachment of the drug could be entertained as an explanation in view of the rapid disappearance of the hyperazotaemia on cessation of the drug treatment; drugs so attached remain fixed for some months. *A. R. D. Adams*

ADRIAENSSENS, K. Nota over de toxiciteit van MEL B in *Trypanosoma rhodesiense* slaapziekte. [**Note on the Toxicity of Mel B in** *Trypanosoma rhodesiense* **Infections**] *Ann. Soc. Belge de Méd. Trop.* 1960, Aug. 31, No. 4, 701–3. Discussion 703–4.

The English summary appended to the paper is as follows:—

"In the treatment of *T. rhodesiense* infections MEL B is active but very toxic. In 55 patients treated by MEL B, 15 complications due to the drug were noted, 10 of which were fatal encephalopathies. The frequency of this complication is lessened by reducing the injected dose but B.A.L. does not seem to be effective against it."

GLASGOW, J. P. **Shinyanga: a Review of the Work of the Tsetse Research Laboratory.** (With an appendix on Tsetse Control by C. F. M. SWYNNERTON, 31–4.) Reprinted from *East African Agric. & Forestry J.* 1960, July, v. 26, No. 1, 22–31. [30 refs.]

With the recent closing of the Tsetse Research Laboratory at Shinyanga, it is fitting that there should be a review of the excellent work achieved there over a period of 37 years. Starting in 1922, with a description of Swynnerton's successful reclamation of western Shinyanga, the author deals with the formation of the Department of Tsetse Research in 1929, and then reviews the results of experiments on late grass burning, fire exclusion, discriminative clearing, game destruction, the biological sterilization of the female tsetse flies, and studies on long-term fluctuations in tsetse numbers; he indicates how Swynnerton's inspiration survived his untimely death in 1938. This paper marks the end of a long chapter in the history of tsetse research.

T. A. M. Nash

YEO, D. & SIMPSON, H. R. **The Effect of Repeated Insecticidal Applications on a Natural Tsetse Population.** *Bull. Entom. Res.* 1960, Nov., v. 51, Pt. 3, 631–7.

The effect of repeated applications of a non-persistent insecticide on tsetse populations is examined mathematically. This is not dissimilar mathematically from problems arising from the introduction of sterile males into a tsetse population. Electronic computation of a suitable programme is used in the present consideration of insecticide effects. The mathematical model for this study is set out in some detail. It is accepted that for *Glossina morsitans* in East Africa the pupal period (of females) lasts 4 weeks, a female lives for 6 weeks, and produces her first larva 3 weeks after emergence and others at intervals of 1½ weeks. Results are tabulated for percentage survival of adult females following 1 to 8 applications of insecticide at different intervals ranging from 1 to 6 or more weeks. This last interval, exceeding 6 weeks, is, in fact, the case where the population is allowed to become stable between treatments.

In discussion of the theoretical expectations and actual experience (by aircraft applications) in the past [this *Bulletin*, 1955, v. 52, 346; 1957, v. 54, 543], there is difficulty in finding explanations universally satisfactory in accounting for certain discrepancy. But, it seems likely that better control would result from making successive applications at 4-, rather than 2-, week intervals. Apart from improved prospects on biological grounds, a single aircraft could accomplish the work. *D. S. Bertram*

LANGE, D. E. & LYSENKO, M. G. *In vitro* **Phagocytosis of** *Trypanosoma lewisi* **by Rat Exudative Cells.** *Exper. Parasit.* New York. 1960, Sept., v. 10, No. 1, 39–42, 1 fig.

When known numbers of washed living *Trypanosoma lewisi* were incubated at 37°C. for 2 hours in a saline dilution of rat peritoneal exudate containing an approximately equal number of cells, phagocytosis of some of the trypanosomes was observed, both in living material examined by phase-contrast microscopy and in stained preparations: the large mononuclear cells were the most active. The proportion of cells which had ingested trypanosomes was increased at least three-fold by the addition to the suspension of serum (at a final concentration of 2·5%) from rats which had been rendered hyperimmune to *T. lewisi* by two inoculations of 140,000 trypanosomes 75 and 83 days after an initial infection from which they had recovered: no increase in phagocytosis followed the addition of normal rat serum or serum taken from rats only 5 days after their infection with *T. lewisi*. Inactivation (at 46°C. for 30 minutes) and, especially, repeated absorption of the serum at 37°C. with living trypanosomes of the same strain reduced or destroyed its enhancing effect. In one experiment serum from convalescent rats 3 months after infection with *T. cruzi* was tested, and was found to enhance phagocytosis of *T. lewisi*, which suggested the presence of some antigen or antigens common to these two species of *Trypanosoma*. *J. R. Baker*

RAY, H. N. & MALHOTRA, M. N. **Akinetoplastic Strain of *Trypanosoma evansi* produced by 'Prothidium'.** [Correspondence.] *Nature*. 1960, Dec. 3, v. 188, 870.

It has been known since early in the century that certain drugs can cause the kinetoplast of some trypanosomes to disappear. Spontaneous loss of this structure has also been reported and the literature on the subject reviewed [this *Bulletin*, 1954, v. 51, 892]. The time taken for disappearance of the structure as a result of drug treatment of various species of trypanosomes has also been recorded by MÜHLPFORDT [*ibid*., 1960, v. 57, 15].

The present authors now report the early loss of the kinetoplast in *T. evansi* as a result of treatment with Prothidium (a phenanthridinium compound) of the young rat host subcutaneously with 0·5 ml. of 0·015% solution of the drug. An akinetoplastic strain, so obtained, has now been maintained for 8 passages at the time of writing. The time required for the kinetoplast to disappear after drug treatment was 44 to 60 hours and in one animal whose blood became free of trypanosomes an akinetoplastic strain appeared during relapse. The new strain multiplied less rapidly than the parent and the rat host lived longer, but finally succumbed. These results are not in accord with the observations of HOARE and BENNETT (*Parasitology*, 1938, v. 30, 529), who considered that the behaviour of the 2 strains was similar.

J. D. Fulton

ELKELES, G. Die Züchtung von *Trypanosoma cruzi* in Gewebekulturen. [**Growth of *Trypanosoma cruzi* in Tissue Culture**] *Ztschr. f. Tropenmed. u. Parasit*. Stuttgart. 1960, v. 11, No. 1, 22–4. [10 refs.]

In this paper the author criticizes the observations of BOCK *et al*. [this *Bulletin*, 1960, v. 57, 798] who found that in the course of development in tissue cultures the leishmanial forms of *Trypanosoma cruzi* pass through a crithidial stage before assuming the trypanosome form. This is contrary to the author's own contention that the leishmanial forms are transformed directly into trypanosome forms. In support of his views, the author quotes Chagas, Mayer and Rocha Lima, Wenyon, Muniz and Freitas, Reichenow and Tang.

[The question dealt with in this paper is highly controversial, for a number of authors (including WENYON, this *Bulletin*, 1926, v. 23, 854), whom the author cites in support of his view) have produced good evidence of the occurrence of crithidial forms in the course of development of *T. cruzi* in the mammalian host. However, the conflicting views could be reconciled if it is accepted that its development may proceed both ways—with or without passing through a crithidial stage, as shown by ROMAÑA (*ibid*., 1957, v. 54, 547).]

C. A. Hoare

MEYER, H. & QUEIROGA, L. T. **Submicroscopical Aspects of *Schizotrypanum cruzi* in Thin Sections of Tissue Culture Forms.** *J. Protozoology*. Utica. 1960, May, v. 7, No. 2, 124–7, 9 figs. [10 refs.]

In a previous paper [this *Bulletin*, 1959, v. 56, 137] a description was given of the ultrastructure of the leishmanial and crithidial stages of *Trypanosoma*

cruzi in thin sections of tissue cultures examined by electron microscopy. This study has been extended to the adult trypanosome stage as it appears in tissue cultures, which forms the subject-matter of the present paper. It was found that the kinetoplast is represented by a spherical vacuole containing a dispersed osmiophilic mass, while the basal granule [=blepharoplast] of the flagellar axoneme lies at the anterior margin of the vacuole enclosing the kinetoplast. Within the cytoplasm of the trypanosomes there is a group of about 11 striae lying between the nucleus and the kinetoplast-blepharoplast complex. This structure, which is likened to the parabasal body of other protozoa and to the Golgi apparatus in metazoal cells, is absent in the leishmanial forms but develops during their transformation into trypanosomes. The appearance of these structures is illustrated in a series of micrographs. *C. A. Hoare*

KAGAN, I. G.; NORMAN, Lois. **Immunologic Studies on** *Trypanosoma cruzi*. **I. Susceptibility of CFW Stock Mice for the "Tulahuen" Strain of** *T. cruzi* [KAGAN & NORMAN]. *J. Infect. Dis.* 1960, Sept.–Oct., v. 107, No. 2, 165–7. **II. Acquired Immunity in Mice infected with Avirulent American Strains of** *T. cruzi* [NORMAN & KAGAN]. *Ibid.*, 168–74. [12 refs.]

These papers describe a series of experiments in which the protective power of culture forms of trypanosomes resembling *Trypanosoma cruzi* was assessed by inoculation into mice which were subsequently given a challenge infection with a lethal strain of *T. cruzi*. The first paper describes careful standardization of the method, especially in assessing the relationship between the dose of organisms and survival time of the mice infected with the lethal strain.

In the second study 7 strains of trypanosomes resembling *T. cruzi* were tested for their protective power against the previously standardized lethal strain. These strains had been isolated from opossums, a raccoon and a skunk which had been trapped in the states of Georgia and Florida [this *Bulletin*, 1960, v. 57, 351], and maintained in the laboratory since 1956.

Under the conditions defined in these papers all these animal strains produced a marked degree of protection against the lethal strain: in this they behaved in the same way as known non-lethal strains of *T. cruzi*, but in a markedly different way from strains of *T. duttoni* and *T. lewisi* which produced no protection against the lethal strain. The authors conclude that these strains are therefore closely related immunologically to *T. cruzi* and may indeed be of the same species, a conclusion which their morphological characteristics also support. *W. E. Ormerod*

RUBIO D., Mafalda. **Natural and Acquired Immunity against** *Trypanosoma cruzi* **in the Hamster** (*Cricetus auratus*). *Biológica*. Santiago. 1959, July–Dec., Nos. 27/28, 95–116, 16 figs. on 4 pls. & 1 chart. [23 refs.]

An account is given of an experimental study on immunity to Chagas's disease in hamsters infected with a strain ("Peru") of *Trypanosoma cruzi*, whose virulence had been enhanced and standardized after passages through inbred mice. Intraperitoneal inoculation of blood forms caused fatal infection in all the hamsters and was accompanied by intense cachexia. The course of

infection differed with the dose of inoculum. Thus, hamsters infected with upwards of 300,000 trypanosomes died within 10–12 days, while those receiving 30,000 died after 18–25 days. In the former case massive invasion of organ tissues took place, but in the latter invasion was slight and numerous degenerate extracellular leishmanoid parasites, surrounded by mononuclear leucocytes (macrophages, polyblasts, lymphocytes and plasma cells), were present. Only the myocardium contained multiplying leishmanial and trypanosome forms, while the development of parasites within histocytes of the subcutaneous tissues was inhibited.

In hamsters inoculated with heavy doses, parasitaemia increased progressively to a high level, in contrast to those inoculated with low doses, in which parasitaemia was low or absent. In the former case the defence mechanism of the host was unable to control the infection, but in the latter a low grade immunity was acquired. However, inoculation of attenuated cultures of the same strain of *T. cruzi* produced in hamsters solid immunity, which protected them for long periods against challenges with heavy doses of blood trypanosomes.

There was evidence that both phagocytosis and antibodies are involved in the defence mechanism against *T. cruzi*. *C. A. Hoare*

HARINGTON, J. S. **Synthesis of Thiamine and Folic Acid by** *Nocardia rhodnii*, **the Micro-Symbiont of** *Rhodnius prolixus*. [Correspondence.] *Nature*. 1960, Dec. 17, v. 188, 1027–8.

LACOMBE, D. Estudos anatômicos e histológicos sôbre a sub-família Triatominae (Heteroptera, Reduviidae). Parte XVII: Estígmas respiratórios de *Triatoma infestans*. [**Anatomical and Histological Studies on Triatominae. XVII. Respiratory Stigmata of** *Triatoma infestans*] *Mem. Inst. Oswaldo Cruz*. 1960, Sept., v. 58, No. 1, 39–58, 19 figs. [36 refs.] German summary.

GOBLE, F. C., BOYD, J. L. & FULTON, J. D. **Effects of Certain Surface-Active Polyoxyethylene Ethers in Experimental Protozoal Infections.** *J. Protozoology*. Utica. 1960, Nov., v. 7, No. 4, 384–90, 6 figs. [25 refs.]

Certain macromolecular polyoxyethylene ethers have been described as having activity against tuberculosis and leprosy in rodents. It has been suggested by MACKANESS [*Bull. Hyg.*, 1954, v. 29, 1258] that this action was exerted through the monocytes which were altered in some way so that the tubercle bacilli contained therein were inhibited or destroyed. Similar compounds with a longer chain length tend to have a pro-tuberculous effect. The present authors studied Triton WR-1339 (a surface-active agent) in which the phenolic groups are arranged in a chain; also LOC-60 (which is pro-tuberculous) and HOC-12½ (which is antituberculous) in which the arrangement is cyclic. WR-1339 and LOC-60 produce gross lipaemia, but HOC-12½ does not.

With WR-1339, doses of 5 gm./kgm. intravenously were tolerated by mice and 1 gm./kgm. daily for 5 days cured infections of *Trypanosoma congolense*

(laboratory strain). The most effective medication was a large single dose 1 day after inoculation of trypanosomes. HOC-12½ was not curative. *T. gambiense* and *T. rhodesiense* (laboratory strains) were less susceptible than *T. congolense;* a strain of *T. rhodesiense* resistant to other drugs showed no extra resistance to WR-1339. LOC-60 was inactive against *T. rhodesiense* and *T. congolense.* Both WR-1339 and HOC-12½ had some activity against *Leishmania donovani* in hamsters, but they had no action against *T. cruzi, Plasmodium berghei, Toxoplasma gondii* or *Leptospira icterohaemorrhagiae.* The trypanocidal action of WR-1339 was diminished by reticuloendothelial blockade with colloidal thorium dioxide or rabbit red cells. During *in vitro* experiments [temperature not stated] *T. congolense* was immobilized and killed by WR-1339 0·05 mgm./ml. in 3½ hours; but HOC-12½ in 50 mgm./ml. dilution had no effect during this time. The serum of rabbits taken 1 day after an intraperitoneal injection of WR-1339 1 gm./kgm. contained 7·5 mgm./ml. and this serum was as actively trypanocidal in mice as an equivalent amount of the compound dissolved in saline. Traces of trypanocidal activity could be found in the rabbit serum for 16 days after injection.

Apparently the curative actions of these compounds against tuberculosis, trypanosomiasis, and leishmaniasis are not parallel one with another. The activity on trypanosomes is probably different from that on tubercle bacilli; it is probably exerted directly on the trypanosomes, and *not* indirectly through the reticuloendothelial system. *F. Hawking*

LEISHMANIASIS

In this section abstracts are arranged as far as possible in the following order:—visceral, cutaneous, muco-cutaneous.

PULVERTAFT, R. J. V. & HOYLE, G. F. **Stages in the Life-Cycle of** *Leishmania donovani. Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Mar., v. 54, No. 2, 191–6, 6 figs. on 2 pls. [21 refs.]

The authors describe the behaviour of leptomonad forms from cultures of *Leishmania donovani* when grown with mammalian cells in a medium composed of the following (%): horse serum 5, rabbit serum 5, Hanks fluid 90, Difco yeast extract 0·1. The cultures were grown in plastic rings attached to a slide and covered with coverslips. The preparations were examined by phase contrast microscopy at 37°C. and photographed cinematographically. The material consisted of (a) monocytes obtained from the peritoneal exudate of mice and hamsters, as well as from serous exudates or bone marrow of human beings; cultures of these were inoculated with leptomonads; (b) macrophages from explants of infected hamster spleen; (c) cell-free cultures of Leishman-Donovan bodies.

In cultures with monocytes, the flagellates were taken up by the phagocytes engulfing them by the posterior extremity. In murine cells the parasites died, but in hamster cells and—to a lesser extent—in human cells they survived and

became rounded. When cultures of normal hamster macrophages and fibroblasts were inoculated with the flagellates, they were not taken up by the cells but survived several days in the medium. In cultures of infected hamster macrophages, the leishmanial forms usually remained inside the cells but those that escaped were phagocytosed. The authors also observed exflagellation of Leishman-Donovan bodies in cell-free cultures. *C. A. Hoare*

Da Cunha, R. Vieira, Xavier, A. F. S. & De Alencar, J. E. Disproteinemia no calazar e suas relações com a reação de fixação do complemento. **[Dysproteinaemia in Kala Azar and its Relations with Complement Fixation]** *Rev. Brasileira Malariologia.* Rio de Janeiro. 1959, Jan., v. 11, No. 1, 45–54, 4 diagrams. [15 refs.] English summary.

Working in the province of Ceará, Brazil, the authors compared the results of (1) the complement-fixation test [CFT], using an antigen extracted from tubercle and "para-tubercle" bacilli [this *Bulletin,* 1958, v. 55, 1313; 1960, v. 57, 573], and the results of paper electrophoresis (31 patients); (2) the CFT and the Napier formol-gel test, since the latter is considered to be closely associated with hypergammaglobulinaemia; (3) the size of the spleen and the gamma-globulin content (47 patients).

No correlation was found between the first two, but there seemed to be some relation between the size of the spleen and the increase of gamma globulin. This increased gamma globulin is interpreted as being due to the reaction of the reticulo-endothelial system to the protozoon; the hypergammaglobulinaemia is independent of the immunity position and probably of the titre of circulating antibody.

The authors suggest that perhaps an antigen extracted from actual *Leishmania* might give a better idea of humoral immunity in this disease.

[The diagrams purporting to show the results obtained, although no doubt statistically accurate, are extremely difficult to understand.]

W. K. Dunscombe

Vavilova, M. P. **[Experimental Infection of Dogs with Two Types of Borovsky's Disease (Leishmaniasis)]** *Med. Parasit. & Parasitic Dis.* Moscow. 1960, v. 29, No. 6, 660–65, 2 figs. [10 refs.] [In Russian.]

The English summary appended to the paper is as follows:—

"According to author's observations dogs in experiment may be infected with both types of skin leishmaniasis; whereby, conforming to clinical observations of leishmaniasis in man, the course of disease in dogs with the II (rural) type is mostly of a shorter duration than in those infected with the I (urban) type of leishmaniasis.

"It was found that in experimentally induced leishmaniasis in dogs leishmaniae may penetrate as far as the regional lymphatic gland and remain within the skin for a considerable length of time, with the clinical process being apparently at its end."

DESTOMBES, P. Application du concept de "systématisation polaire" aux leishmanioses cutanées. [**A "Polar Conception" of the Lesions of Cutaneous Leishmaniasis**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 299–300.

The author points out that the intradermal reaction (Montenegro) is negative in diffuse forms of dermal leishmaniasis and positive in localized forms. There is thus a parallel with the Mitsuda reaction in lepromatous and tuberculoid leprosy. He suggests that the variation in the clinical aspects of dermal leishmaniasis may result from variation in host response to the same organism and need not necessarily be related to variations in species of parasite. *B. G. Maegraith*

BALZER, R. J., DESTOMBES, P., SCHALLER, K. F. & SÉRIÉ, C. Leishmaniose cutanée pseudolépromateuse en Éthiopie. [**"Pseudolepromatous" Cutaneous Leishmaniasis in Ethiopia**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 293–8, 8 figs. on 4 pls. [11 refs.]

A young male Ethiopian from an area 400 km. north of Addis Ababa presented with extensive lesions of the feet, arms and face. The lesions of the feet (where the condition started 11 years before) resembled mycetoma with elephantiasis. Lesions on the soles resembled yaws. Those of the face and arms were diagnosed as being due to lepromatous leprosy, although no leprosy bacilli were found in the granulomatous tissue. Sulphones had no therapeutic effect. On careful examination *Leishmania* spp. were found in large numbers in biopsy material from lesions on the forearm, face and skin of the feet. The spleen was not enlarged. The bone marrow was depressed and contained no *Leishmania;* the leucocyte count was 2·15 thousand cells per cu. mm. (lymphocytes 42%). The strain of *Leishmania* from this patient has been cultured but not identified. Treatment with urea stibamine was followed by a severe acute reaction.

The diffuse nature of the lesions suggested post-kala-azar cutaneous leishmaniasis, but kala azar was not known in the family or community from which the patient came. The absence of involvement of the reticulo-endothelial system was also not in favour of the causative agent being *Leishmania donovani.* The diffusion of the lesions did not support the view that *Leishmania tropica* was the aetiological agent.

The picture more closely resembled the effects of *L. brasiliensis,* but this species is unknown in Africa. The authors suggest that a review of *Leishmania* spp. is necessary. *B. G. Maegraith*

JAFFÉ, L. **Further Observations on Leishmaniasis Americana of the Upper Respiratory Passages in Panama.** Reprinted from *Arch. Otolaryngol.* 1960, Oct., v. 72, 464–70, 2 figs.

These 26 patients were examined in Panama during the years 1954–59. There were 12 males and 14 females, in age range from 5 to 75 years, and

comprised mestizos, Negroes and Panamanian Indians. The author had previously reported 8 cases of nasal leishmaniasis in Panama [this *Bulletin*, 1955, v. 52, 962; 1956, v. 53, 660].

The investigations included otolaryngological examination, chest films, X-ray examination of the paranasal sinuses and in most subjects serological tests for syphilis. The intracutaneous Montenegro test for leishmaniasis was carried out in 25 patients and was positive in all. Suspicious skin scars suggesting former leishmanial cutaneous lesions were found in 7.

The otolaryngological findings were as follows:

(1) unilateral or bilateral crusting of the anterior septum, often with fine granulations, in 6 patients;
(2) granulations upon the inferior turbinates or the anterior septum or both in 6 patients; in 2 of these the VDRL tests were positive;
(3) in one patient a broad, sessile, unilateral polyp on the anterior part of the septum;
(4) ulceration of the anterior septum, without perforation, in 2 patients;
(5) perforated septa with active lesions in 3 patients;
(6) smooth perforations of the anterior septum without active lesions in 4;
(7) affection of the external nose by scarring and sinking in or both with septum perforations in 3; one other patient of this group presented an enormous destruction of the interior nose with ozaena and myiasis (live larvae resembling those of *Cochliomyia americana*);
(8) affection of the nose, oropharynx and larynx in one patient.

In one severe case of muco-cutaneous leishmaniasis with affection of the larynx *Leishmania brasiliensis* was discovered in histological sections of the mucosa. The lesions of the upper respiratory tract healed promptly with stibophen therapy.

These observations in only one province of the Republic of Panama show that leishmaniasis of the upper respiratory passage is much more common in this country than it was thought to be, but it is as dangerous there as in other South American countries. However, the fact that some patients presented a smooth perforation of the anterior septum without any fresh lesion, and a strongly positive Montenegro test with a negative VDRL, suggests that spontaneous healing may occur.

It does not appear safe to trace all signs and symptoms to one infection only, as multiple infections are frequent.

The author's methods of treatment have remained unchanged: stibophen (a trivalent compound known as Neoantimosan, Fouadin, or Reprodal) was used in all cases. The results were good, but only if 10 to 16 injections were given in one series and if this regime was repeated, if necessary, after a lapse of one or more months. Untoward reactions continue to occur occasionally, but never severe enough for omission of treatment. Should malaise or pain become pronounced, the daily dose should be reduced. Unfortunately, cooperation on the part of the patient is often lacking.

Full details are given of 8 cases.

[The complete details of the second reference quoted above were not available to this *Bulletin* at the time. The textbook *Otolaryngology*, was edited by G. M. Coates *et al.* and published by the Prior Co. Inc., Hagerstown, Maryland.] *Philip Manson-Bahr*

FURTADO, T. A., CISALPINO, E. O. & SANTOS, U. M. *In vitro* **Studies of the Effect of Amphotericin B in** *Leishmania brasiliensis*. *Antibiotics & Chemotherapy*. New York. 1960, Nov., v. 10, No. 11, 692–3.

The authors, from the Faculty of Medicine of the University of Minas Gerais, Brazil, studied the effect of amphotericin B in falling concentrations of 500, 100, 10, 1·0, 0·1 and 0·01 μgm./ml. on a recently cultivated strain of *Leishmania brasiliensis*. The amphotericin was incorporated in the culture medium (2% aqueous dextrose and Rugai's modified medium) and an inoculum of 16,000 leishmaniae per ml. was added. Incubation was carried out at 22° to 24°C. for 20 days and the cultures were examined daily for viability. 12 assays were performed for each concentration.

To verify the action of the drug the cultures were centrifuged at 2,000 r.p.m. for 20 minutes and the sediment placed in saline: this process was repeated 3 times to eliminate all trace of the antibiotic. The final sediment was incubated under similar conditions on fresh culture media without the antibiotic and the cultures were examined daily. Viable strains were treated similarly as controls.

All media showed complete absence of growth in concentrations of amphotericin B from 500 to 0·1 μgm./ml. With 0·01 μgm./ml. only 10% of leishmaniae were viable on the first day and none on the second. Normal reproduction occurred in the control tubes. Consistent results were obtained in the transplant experiments. *H. J. O'D. Burke-Gaffney*

FEVERS OF THE TYPHUS GROUP

In this section abstracts are arranged as far as possible in the following order:—general; louse-borne typhus, flea-borne typhus, mite-borne typhus; rickettsialpox; tick-borne typhus; Q fever, other rickettsial diseases.

ERRATUM

In the abstract of the paper by JUMINER, this *Bulletin*, 1961, v. 58, p. 44, line 2, for "*Rickettsia norvegicus*" read "*Rattus norvegicus*."

MAROJA, O. A reação de Weil-Felix em soros provenientes de Belém e outras localidades da Amazônia. [**The Weil-Felix Reaction in Sera from Belém and other Parts of Amazonia, Brazil**] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1960, June, v. 11, No. 1, 225–9. English summary (8 lines).

No positive results at significant titres were obtained with 159 sera from febrile patients in 16 localities.

GAMET, A. & MARTIN, J. P. De l'importance et de la diversité des aspects cliniques et sérologiques des rickettsioses au Cameroun. [**Significance and Diversity of Clinical and Serological Factors in Rickettsial Infections in the Cameroons**] *Med. Afrique Noire.* Dakar. 1960, Nov. 1–15, v. 7, No. 21, 436–7. [10 refs.]

During a period of 3 months, 50 patients seen at the hospital at Yaoundé were diagnosed by means of microagglutination tests as suffering from rickettsioses. These patients presented a variety of clinical syndromes, classified as pseudo-influenzal (19), " boutonneuse " [with maculo-papular eruptions] (8), typhoidal (8), and " *formes frustes* " [with no definite symptoms other than asthenia] (7); 6 patients with uveitis and 2 with generalized muscle and bone pains were considered to be suffering from sequelae of rickettsioses. In the microagglutination test, 43 sera reacted with epidemic-type rickettsial antigens (titres ranging from 1 in 320 to 1 in 5,120); 22 reacted with murine antigens (1 in 80 to 1 in 1,280); and 7 with boutonneuse antigens. No serum reacted with Q fever antigens at a titre of 1 in 20.

It is concluded that the rickettsial microagglutination test should be employed as a routine diagnostic procedure in the tropics. *R. S. F. Hennessey*

DELANOE, G. Rickettsioses et affections cardiovasculaires (à propos de 13 observations, dont 12 cardiopathies). [**Rickettsial Disease and Cardiovascular Lesions**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 216–41, 4 figs. on 2 pls. [37 refs.]

The author reviews the literature on cardiac involvement in rickettsial infections. He describes the results of slide microagglutination (with 5 antigens) in 30 patients in Morocco presenting with obscure cardiac or vascular disturbances. Of these, positive results were given with one or more antigens in 13 cases, including endocarditis, myocardial infarction and phlebitis. Positive agglutinations were recorded as follows: *Rickettsia prowazeki,* 9; *R. mooseri,* 4; *R. burneti,* 1 and *R. conori,* 1. Because of the importance of making the diagnosis of rickettsiosis, especially in regard to prognosis, the author advises the use of slide agglutination and other methods in all obscure cases of vascular or cardiac disease. Lesions may develop in rickettsial infections as a primary result of the infection, during a recrudescence or following the stress of some other infection.

Full details are given of the 13 patients who were positive.

B. G. Maegraith

IABLONSKAIA, V. A., KOVREVA, T. S. & YEREMENKO, A. V. **Epidemiology of Typhus. I. Material of the Serological Diagnosis of Typhus.** *Problems of Virology.* London. 1960, v. 5, No. 2, 257–61. [Translated from Russian.]

Of 184 cases of typhus fever studied in 1957–58 [? in Moscow], 88 (48%) were primary infections and 96 (52%) were recurrences; only 3 recurrences were in persons aged less than 31 years and 70 were in persons aged more than 51. In 173 cases (94%) typhus was diagnosed or suspected on clinical grounds before serological tests were undertaken; 11 were diagnosed solely

on serological grounds. Complement-fixation and haemagglutination tests for antibodies to *Rickettsia prowazeki* were both positive in 182 patients, one test being positive in each of the 2 remaining patients. Haemagglutination titres were between 1 in 250 and 1 in 32,000, and complement-fixing titres between 1 in 80 and 1 in 5,120. The Weil-Felix test with *Proteus OX19* antigen was positive at a titre of 1 in 100 in 53 out of 72 sera examined.

Sera from 142 patients with diagnoses other than typhus fever all gave negative haemagglutination tests for antibodies to *R. prowazeki*; 12 sera had titres between 1 in 10 and 1 in 40 in the complement-fixation test.

R. S. F. Hennessey

Fleck, L., Porat, Sara, Evenchik, Z. & Klingberg, M. A. **The Renal Excretion of Specific Microbial Substances during the course of Infection with Murine Typhus Rickettsiae.** *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 351–61, 2 figs. [25 refs.]

Samples of urine (concentrated about 10-fold by dialysis) from guineapigs infected with *Rickettsia mooseri* contained substances which reacted with rabbit antiserum for *Proteus OX19* and with convalescent serum from murine typhus patients, causing inhibition of agglutinating activity against red blood cells sensitized with *Proteus OX19* polysaccharides or with antigenic material from *R. mooseri*. At least 2 specific substances, presumably originating from degraded *R. mooseri*, appeared to be present; one reacted with both anti-*OX19* serum and convalescent serum, inhibiting agglutination of cells sensitized with *OX19* polysaccharides, and induced formation of agglutinins for *Proteus OX19* in rabbits but not in guineapigs; the other reacted only with convalescent serum, inhibiting agglutination of cells sensitized with antigens from *R. mooseri*, and was antigenic in both rabbits and guineapigs. Excretion of the first-mentioned substance began about 2 days before the onset of fever and persisted for several weeks; the substance was detectable when latent infections were present.

A substance which reacted with *OX19* antiserum to cause inhibition of agglutination of red cells sensitized with *OX19* polysaccharide was also found in the urine of 10 out of 19 patients suffering from murine typhus; it was present in the urine of all of 5 patients examined in the first week of illness, and the authors consider that detection of excretion of antigen by this method may be useful in the early diagnosis of typhus.

[See also this *Bulletin*, 1947, v. 44, 1057; 1950, v. 47, 976.]

R. S. F. Hennessey

Chrzanowski, J., Kularska, Irena, Stempien, R. & Wojciechowski, L. Badania serologiczne w kierunku goraczki Q wśród pracowników przemysłu wełnianego. **[Q Fever among Workers of the Woollen Industry. Serological Investigations]** *Przegląd Epidemiol.* Warsaw. 1960, v. 14, No. 4, 411–16. [23 refs.]

The English summary appended to the paper is as follows:—

"Workers of 5 textile plants in Łódz and Czestachowa were placed under epidemiological observation for Q fever during two years (1958–1959). These

observations were undertaken since the wool used in these factories was imported from countries endemic and enzootic to Q fever (Australia, Egypt, China and Argentina).

"In 12 of 504 people examined with the complement fixation test—R. burneti (Henzerling)—Q fever was found in a titre from 1:8 to 1:32. These included 9 cases of workers in the wool sorting department, most exposed to the inhalation of wool dust as well as 2 workers in the laundry and 1 in the store room. No epidemics resembling Q fever had been confirmed in these departments in the past except during influenza periods."

TOKAREVICH, K. N. & VASIL'EVA, L. D. **Study of Q Fever in Leningrad and the Leningrad Region.** *Problems of Virology*. London. 1960, v. 5, No. 1, 75–81. [Translated from Russian.]

This paper describes some epidemiological features of 336 cases of Q fever recorded in Leningrad during the period 1954–58 and of 152 cases seen in the Luzh district (Leningrad region) during 1956–58.

In Leningrad, most of those affected had been working in industries which brought them into contact with cotton or cotton wastes (120 persons) or with hides, wool and meat (118 persons). Some of the cotton had come from areas where Q fever was enzootic, but how it had become contaminated was a matter for speculation. In cotton processing factories, infections were commonest among workers exposed to large amounts of dust. Cases occurred singly and in groups, with no seasonal fluctuation.

The source of infection in the Luzh district appeared to be cattle; in complement-fixation tests for Q fever antibodies, 28·4% of sera from 351 animals gave positive results. The incidence of cases was markedly seasonal, and the results of serological surveys suggested that the focus was of relatively recent origin. *R. S. F. Hennessey*

ALLISON, A. C. & PERKINS, H. R. **Presence of Cell Walls like those of Bacteria in Rickettsiae.** *Nature*. 1960, Dec. 3, v. 188, 796–8, 1 fig. [17 refs.]

Cell-wall preparations of *Rickettsia burneti* were not morphologically changed by treatment with trypsin; digestion with egg-white lysozyme resulted in the disappearance of morphologically recognizable cell walls, as occurs when Gram-negative bacteria are treated with this enzyme. Suspensions of *R. burneti* which had been treated with lysozyme contained material giving the Morgan-Elson reaction for N-acetyl amino-sugars. Chromatographic analysis of hydrolysates of suspensions of *R. burneti* revealed material which was identical with muramic acid. Preliminary tests have also shown that muramic acid is present in *R. typhi* [*R. prowazeki*] and in the mouse pneumonitis organism (psittacosis-lymphogranuloma group). No trace of muramic acid was detectable in suspensions of vaccinia virus or influenza virus.

From these results, it is concluded that rickettsiae have cell walls similar to those of bacteria. This and other points of difference between the rickettsiae and true viruses (including the presence in rickettsiae of both DNA

and RNA, their multiplication by binary fission, and their sensitivity to antibiotics such as chloramphenicol and the tetracyclines) suggest to the authors that rickettsiae are probably bacteria that have become adapted to intracellular multiplication. *R. S. F. Hennessey*

SMITH, W. G. & EVANS, A. D. **Chronic Q Fever with Mitral-Valve Endocarditis.** *Lancet.* 1960, Oct. 15, 846–8.

In patients exhibiting the clinical picture of infective endocarditis but with negative blood cultures, rickettsial infection should be considered. The authors describe a case in point in a patient in whom rheumatic mitral stenosis was diagnosed in 1951. A series of febrile episodes associated with signs of endocarditis followed after about 7 years and serological evidence of infection with *Rickettsia burneti* was obtained a year later (presumably complement fixation). Treatment with antibiotics (oxytetracycline followed by erythromycin and chloramphenicol) had good results but the patient subsequently died after valvotomy. At autopsy the mitral valve was found to be thickened and fibrosed; an organizing thrombus was present in the area, and in the inflammatory reaction beneath, *Rickettsia*-like bodies were found. Suspensions of the vegetations were inoculated into guineapigs the sera of which later developed complement-fixing bodies against *R. burneti.*

The authors consider that the patient was suffering from chronic Q fever. [See also DELANOE, p. 434, above.] *B. G. Maegraith*

YELLOW FEVER

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

HANNOUN, C. & PANTHIER, R. Application de la méthode des plages en cultures cellulaires à l'étude du virus-vaccin amaril 17D. [**Application of the Plaque Technique to the Study of 17D Yellow Fever Virus**] *Bull. Soc. Path. Exot.* 1960, May–June, v. 53, No. 3, 424–30, 7 figs. on 2 pls.

Chick embryo tissue monolayers were prepared as described by PORTERFIELD [this *Bulletin*, 1960, v. 57, 363]. Different periods of incubation of the inoculum on the monolayer before overlaying were tried, and the maximum number of plaques was found with 7 hours' incubation. An inoculum of 0·1 ml. volume was found to allow parts of the monolayer to dry—0·5 ml. was found to be better and to give higher plaque counts. Higher plaque counts were also obtained when the virus inoculum was suspended in Hanks solution than in culture growth medium and the addition of ascorbic acid or cysteine to the Hanks solution reduced the plaque count. By these methods plaques were found to appear after 4 days' incubation and were maximum

in number and size by the 7th day. They were 0·5–2·0 mm. in diameter with somewhat irregular margins. Material containing 6·5–7·1 log plaque-forming units per ml. was found to contain 6·8 log LD50 for mice so that the titres were identical. Material from plaques was ground up and inoculated into mice. [From limited data] it appeared that the titre was highest on the 4th and 5th days, diminishing thereafter. Microscopic examination of plaques revealed degeneration followed by re-invasion of the area by neighbouring cell proliferation. *C. E. Gordon Smith*

RABIES

BOULGER, L. R. & HARDY, J. **Rabies in Nigeria.** *West African Med. J.* 1960, Dec., v. 9 (n.s.), No. 6, 223–34, 3 figs. [13 refs.]

After tracing the development of the Rabies Service within the Federated Medical Laboratories at Yaba, the authors give: (i) a general picture of the occurrence and distribution of human and animal rabies throughout the Federation of Nigeria during the years 1928 to 1959; (ii) a review of canine rabies in the Lagos area between March 1956 and December 1959; and (iii) a statement on the production method for the rabies vaccine intended for human prophylaxis in the Federation.

(i) Between 1928 and 1959 the Research Laboratory at Yaba received 2,749 animal brains and 90 human brains for the diagnosis of rabies. Of the animal brains 2,470 (89·9%) derived from dogs, 208 (7·6%) from cats and the remaining 71 mostly from other domestic species. Of the 2,659 brains found suitable for examination 1,100 proved positive for rabies: 1,046 (95·1%) from dogs, 48 (4·4%) from cats, 4 (0·3%) from goats, 1 (0·1%) from a donkey and 1 (0·1%) from a pig. No confirmed case of rabies in any wild animal was discovered. The dog was thus shown to be the principal vector of rabies in a country where since 1928 the distribution of laboratory-confirmed animal rabies has been widespread. Of the 90 human brains received 79 derived from clinical cases of rabies, 52·5% of these cases having occurred in children. A definite history of dog bite was given in 82% of the cases and in no instance was any other species of animal incriminated. The diagnosis of clinical rabies was confirmed in 37 (50%) of the 74 brains, on which it was found possible to carry out either or both the microscopic examination and the mouse inoculation test, but only 22 (29·6%) of the specimens showed Negri bodies and from only 20 (27·1%) was rabies virus isolated. During the period under review there were 120 notifications of human cases of clinical rabies, the geographical distribution of which was widespread.

(ii) In the Lagos area, where of all laboratory-confirmed cases of animal rabies 91·5% were found to occur in dogs, analysis of such canine cases as had a history of clinical symptoms showed 68% to have been affected by the dumb form of the disease. A study of the relation of 38 clinical cases of canine rabies to the occurrence of Negri bodies in the brain and the presence

of street virus in the brain and salivary gland showed: that Negri bodies were seen in 16 (59·3%) of 27 dogs with dumb rabies and in 8 (72·7%) of 11 with furious rabies; that virus was present in the brain in 24 (88·9%) of 27 and in 8 (72·7%) of 11 dogs affected, respectively, by dumb and furious rabies; and that virus was present in the salivary gland in 21 (77·8%) of 27 dogs with dumb rabies and in 8 (72·7%) of 11 with furious rabies. The percentage of microscopically negative brains found positive on mouse inoculation of brain and salivary gland was 33·3 and 23·1, respectively. The mean incubation period for mice inoculated with salivary gland material was 10·9 days, as compared with one of 15·7 days in mice inoculated with brain suspension.

(iii) The rabies vaccine produced at Yaba for human prophylaxis is a sterile preparation of inactivated virus in 0·5% phenolized physiological salt solution; it consists of a 4% brain suspension from sheep infected intracerebrally with fixed rabies virus (Paris strain). Vaccine for dog and cat prophylaxis is prepared at the Veterinary Research Laboratories, Vom. *G. Stuart*

Szlamp, E. L. **An Outbreak of Rabies in Ngamiland.** *J. Trop Med. & Hyg.* 1960, Nov., v. 63, No. 11, 264–5.

Rabies is enzootic in Ngamiland, Bechuanaland, with reservoirs in domestic and feral animals and occasionally sporadic outbreaks in domestic dogs and cattle. As a result of such a small outbreak at the end of 1958 antirabies vaccine was given to 51 human beings at the hospital in Maun. 2 cases of human rabies occurred and although the patients were bitten on the extremities, the incubation period was less than 40 days. The cases are described.

The first patient was an African of 25, bitten on the Achilles tendon by a puppy which died undiagnosed 2 days later. After an incubation period of 39 days the patient eventually died: "his condition was diagnosed as rabies", but no further details are given.

An adult European woman was bitten on the thumb by her pet puppy, which was killed next day. A fortnight later a report from the veterinary laboratory at Onderstepoort confirmed that the dog had suffered from rabies and the patient was given a course of rabies vaccine. She soon developed urticaria which was treated with cortisone acetate and disappeared in 24 hours, but on the 19th day of the course she was admitted to hospital with severe pain in the opposite arm and shoulder. Stiffness of the neck, pain in the other arm and muscular weakness in the arms and neck occurred. Symptoms of transverse myelitis developed and were followed by respiratory paralysis. The patient died on the 39th day after the bite. Demyelinization of the nerve tracts in the brain and spinal cord was confirmed at autopsy and Negri bodies were found in the brain. It is suggested that the demyelinization was due to the antirabies inoculation, though none of the other 50 patients developed side effects. It is noted that this condition was not prevented by the cortisone treatment which had been given on the last 19 days of vaccination.

The veterinary officer believed that the virus in this outbreak had produced a somewhat atypical picture in dogs and it is suggested that the virus itself may have produced some of the manifestations in the human patient, who had shown few symptoms of clinical rabies. *H. J. O'D. Burke-Gaffney*

COCHAVY, Z. & DAVIES, A. M. **Animal Bites in Israel. An Epidemiological Analysis with special reference to the Problem of Rabies.** *J. Trop. Med. & Hyg.* 1960, Nov., v. 63, No. 11, 251–7, 7 figs. & 1 diagram.

In Israel during the 6-year period 1954–59 the annual number of persons bitten by domestic or wild animals suspected of rabies averaged 7,489. The almost daily occurrence of these animal bites, in a country where rabies has long been enzootic among its wildlife population, led the authors, in their search for causes and means of prevention, to make an analysis of the human, animal and environmental factors involved in the biting incidents reported during 1959. The results of their analysis are given in the present paper.

During 1959, when of 5,232 animals examined for rabies 50 (0·95%) proved to be positive, the number of human beings scratched or bitten by wild or domestic animals totalled 6,944—a figure which, in a population of 2,031,672, showed an attack rate of 34·1 per 10,000: 43·1 for males and 24·9 for females. These rates, which rose to a summer peak, showed considerable variation between the different districts, being highest in agricultural areas in the central part of the country; they also varied with the type of residence, being highest, at 691 per 10,000, in temporary settlements in rural areas and lowest, at 27·1, in urban areas. The rates were highest in children at ages 5–14 years, being more than twice as high in that age-group as those at other ages; at all ages the rates in males were at least double those in females.

Of the 6,944 bites and scratches reported 84% were inflicted by domestic animals, mostly by dogs and cats, and 16% by stray animals; 2,923 (42%) resulted from aggravation of the animals, the number being greatest among children of school age; 46·1% were situated on the legs and 39% on the arms, these proportions being reversed in bites resulting from aggravation; one-third to one-half of all bites were superficial, 18–30% of medium severity and 6–14% sufficiently severe to necessitate surgical treatment.

To ensure a reduction in the incidence of animal bites, education, particularly of the school child, in the habits and care of domestic animals is undoubtedly necessary: avoidance of aggravation, for example, would reduce incidence from 34·1 to 19 per 10,000. A significant reduction would also be effected by enforcement of the licensing laws and destruction of all stray animals.

G. Stuart

HELD, J. R., TIERKEL, E. S. & ARNSTEIN, P. Análisis epidemiológico de la rabia humana y animal en Estados Unidos. [**Epidemiological Analysis of Human and Animal Rabies in the United States**] *Bol. Oficina Sanitaria Panamericana.* 1960, Nov., v. 49, No. 5, 456–61, 7 figs.

Rabies has been recorded in the United States since 1753 and in 1909 it was notified in every state except 9, these exceptions being chiefly in the north-west. In 1959, cases occurred in every state except 10 and in general the same states were exempt: the largest numbers occurred in Texas (567), New York (478) and Alabama (271). A table shows the origin of 4,117 cases: only 6 were in human beings, 1,124 were in dogs, between 700 and 920 were in skunks, foxes and cattle, 310 in cats and 85 in bats. Smaller numbers

occurred in other animals. The dog is the principal domestic animal affected and foxes and skunks predominate among the feral animals with rabies.

A figure shows the decrease in incidence over the 20 years 1939–1959. Although there was a great reduction of incidence in dogs (by 87%) because of suitable methods of control and public education, there was an increased incidence in feral animals. The decreased incidence in dogs is all the more striking since the number of dogs rose from 12 million to 25 million between 1946 and 1956.

A sketch map shows that the incidence of rabies in foxes is greatest in the south-east and Gulf of Mexico region, but extends north-east as far as New York. On the other hand rabies in skunks affects the states in the Great Plains and the central Californian valley. There is a current epizootic, affecting principally *Mephitis mephitis,* which was recorded in Iowa in 1945 and has since spread to neighbouring states. Rabies in wild animals is important not only directly but because these animals serve as a reservoir for domestic dogs and cattle.

Rabies in insectivorous bats was first recorded in Florida in 1953 and since then the virus has been isolated from bats in 24 states: the incidence is probably greater than that reported.

The greatest mortality from rabies in man in the United States was in 1890 when there were 143 cases. From 1900 to 1959, there were 3,085 deaths, with an annual average of 51. Between 1940 and 1959 the incidence in man varied from 56 in 1944 to 5 in 1955, but there has been a general decrease in the last 20 years. Between 1946 and 1956 there were 212 human deaths from rabies, most of them in the south. Epidemiological data are available for 147 of these cases. Half of them occurred in children under 15 years of age and 21 of these had resulted from bites on the head and face: in those over 15 years only 8 were due to bites on the head; males were affected more frequently. All these factors point to the greater susceptibility and greater opportunity for contact with animals and for bites near the head in young children: the great majority of bites in these cases were by dogs.

In 109 cases where the data were available the incubation period was seen to vary from 6 to 270 days with an average of 38. The usual experience was noted that the period was shorter in those who were severely bitten. Details are given of these features.

None of the 147 patients had received antirabies vaccination before exposure and only 40 after it. In 30 of these the incubation period was not more than 30 days and in 17 the first symptoms appeared during treatment or on the day after the last injection. 22 patients received immediate treatment, 12 received it within 1 to 4 days and 6 in 8 to 21 days. It was concluded that vaccination could not be expected to protect those having an incubation period of less than 30 days: details are given.

Evidently, rabies is widespread in the United States and many species of animals are involved. Reduction of the incidence in man is linked with control of these animals: the steady decrease is to be attributed to the control of dogs, the major source of infection, and to public health education which has increased the awareness of the people. Since the incidence in man has fallen to 6 cases annually in the last 3 years it is hoped that control measures may eliminate human rabies from the United States. [See also this *Bulletin,* 1960, v. 57, 701, 703.] *H. J. O'D. Burke-Gaffney*

SCATTERDAY, J. E., SCHNEIDER, N. J., JENNINGS, W. L. & LEWIS, A. L. **Sporadic Animal Rabies in Florida.** *Pub. Health Rep.* Wash. 1960, Oct., v. 75, No. 10, 945–53, 3 figs.

In Florida during recent years the continued occurrence, among household animals and wildlife, of sporadic cases of rabies, *i.e.* cases isolated in time and space from other rabies infections, led the authors to undertake intensive investigations to determine whether or not there existed in that State an inapparent reservoir serving as a source for the spread of the disease. To this end all available data were collected and examined with respect to dogs, household cats, foxes, raccoons and skunks, diagnosed as rabid in the laboratories of the State Board of Health.

Because of lack of data the attempted study of sporadic cases in dogs proved unproductive. Epidemiological investigation of rabies in household cats in peninsular Florida failed to reveal evidence of the disease in any other animal; rabid cats in that terrritory would appear, therefore, to have acquired a truly sporadic infection. In this connexion data on 9 rabid kittens less than 7 months old suggested some small animal as a reservoir, perhaps one brought to kittens by mother cats and used for practice in hunting, *e.g.* rat, mouse or bat. Rabies has not, however, been reliably reported from native rats and mice in Florida, but the yellow bat, *Dasypterus floridanus,* has been found to have an infection rate of about 2% in nature and to be one of the most powerful biters among Florida bats. Among foxes there was no clear seasonal trend in the sporadic cases, which in peninsular Florida between 1951 and 1958 numbered 18 and were not correlated with any other rabies cases. Weight of evidence suggested that among foxes sporadic cases were caused by an effective contact with an inapparent reservoir. It is noteworthy that sporadic infections were not reported from the epizootic fox rabies areas along the Georgia and Alabama borders, where 2 known epizootics occurred in adjacent areas of the 3 states. Rabies in raccoons occurs only in peninsular Florida, where it spreads along the major waterways as an enzootic and where the sporadic reporting of cases is due to the inapparent nature of the infection among these animals, so unaggressive when rabid. Data failed to show that raccoons had had any contact with an inapparent rabies reservoir in other species, the wide distribution and sporadic reporting of cases making it virtually impossible to recognize any such contact. Data on skunks were meagre, only 9 cases among these animals having been recorded since 1951, but the infrequency of attacks by rabid skunks would seem to exclude these animals from consideration as the effective, inapparent rabies reservoir sought by the authors.

From the available data certain general impressions may be gathered concerning the existence of an inapparent rabies reservoir in Florida. The epizootics observed in foxes and the enzootic spread seen in raccoons may explain all the rabies cases recorded from western Florida and some of the sporadic cases in peninsular Florida. As, however, some of the sporadic cases, especially in kittens, could not possibly be traced to wounding by raccoon, fox or dog, it is logical to assume that some other vector is responsible, at least for some of these cases—a vector, which presumably may infect cats and other species. Whether insectivorous bats, recently proved by BELL [this *Bulletin,* 1959, v. 56, 1023] to be infective, can act in this capacity is not yet known, but there is little room for doubt that some wildlife reservoir for rabies exists in

Florida. Its identity and the means of the spread of the infection, however, need to be determined by further study. *G. Stuart*

KENT, J. R. & FINEGOLD, S. M. **Human Rabies transmitted by the Bite of a Bat: With Comments on the Duck-Embryo Vaccine.** *New England J. of Med.* 1960, Nov. 24, v. 263, No. 21, 1058–65, 1 fig. [51 refs.]

5 human deaths from rabies attributed to exposure to infected insectivorous bats have been previously reported [this *Bulletin,* 1960, v. 57, 587, 895]. In 4 of these cases bat transmission was based on epidemiological and anamnestic evidence and in one, in which the biting bat was available for laboratory investigation, rabies virus was isolated and identified from the brain of both bat and human victim. The case now reported is assumed to have been due to infection by an insectivorous bat and is, therefore, the sixth such case.

The victim, a 53-year-old man, had, between 9 April and 1 May, 1959, investigated caves in northern Mexico and southern Texas as possible commercial sources of bat guano deposits. No definite history of bat bite or other source of infection was established, but the man had in the course of his work come in contact with many bats, which flew or brushed against him. Between 22 and 31 May he experienced pain in the left arm, numbness in the left hand, anorexia, retching, dyspnoea and chest pain. He was admitted to hospital on 1 June with a tentative diagnosis of myocardial infarction. While in hospital he became gravely ill, with continuous retching, hypersensitivity, anxiety and increasing mental confusion and, later, with foaming at the mouth and hydrophobia. A clinical diagnosis of rabies was made on 2 June and the patient died on the following day. Biological tests on mice revealed the presence of rabies virus in the victim's brain (hippocampus) and cerebrospinal fluid; identity of the virus was confirmed by serum-virus neutralization tests.

The diagnosis, in this case, of rabies transmitted by an insectivorous bat is, of course, presumptive, being based on circumstantial evidence. Transmission of the infection by vampire bats can be ruled out, as the areas in Mexico visited by the victim were at least 50 miles north of the northernmost point where vampires have been reported. Moreover the clinical features of this case, in common with those in the other 5 cases of human rabies transmitted by insectivorous bats, were indistinguishable from those observed in human rabies from other sources, *e.g.* dogs, cats, foxes, skunks, and quite different from those occasioned by vampire bite, *viz.,* an ascending Landry type of paralysis following on the numbness and other sensory phenomena experienced at the bitten site. In this connexion it is of interest to note that the virus isolated from insectivorous bats has been found to be considerably more virulent than the strain currently present in vampire bats—a finding which supports the belief that North American insectivorous bats do not contract their infection from vampires during their winter migration into Mexico and their cohabitation in roosting places there.

After a comprehensive review of the relevant literature, a detailed account of the present status of rabies in the insectivorous *Chiroptera* of the United States, and a discussion on the possible role played by these bats in the epidemiology of the disease there, the authors consider the prophylactic value of rabies vaccine of duck-embryo origin [*ibid.,* 1955, v. 52, 970]. This vaccine,

being substantially free from the encephalomyelitic factor (myelin) present in rabbit-brain vaccine, might, it was hoped, confer satisfactory immunity, without the risk of allergic encephalomyelitis occasionally seen in patients treated with, *e.g.*, Semple-type vaccine. Already over 5,000 bitten persons have been protected by duck-embryo vaccine, without the occurrence of any neurological complications; moreover this vaccine has proved of undoubted service in the restimulation of immunity induced by previous Pasteur treatment. *G. Stuart*

McQueen, J. L., Lewis, A. L. & Schneider, N. J. **Rabies Diagnosis by Fluorescent Antibody. I. Its Evaluation in a Public Health Laboratory.** *Amer. J. Pub. Health.* 1960, Nov., v. 50, No. 11, 1743–52, 5 figs.

Brain specimens were stored in the dry state, chilled or frozen, until tested. Paired impression smears were made on slides, allowed to dry, then fixed for 4 hours in acetone at −20°C. For staining the 2 impressions were ringed with vaseline. To one of them was added hyperimmune serum conjugated with fluorescein isothiocyanate mixed with an equal volume of normal mouse-brain suspension: to the other was added the conjugated serum mixed with the same proportion of a suspension of mouse-brain infected with rabies. The slides were incubated at 37°C. for 30 minutes, washed in phosphate-buffered saline and mounted in buffered glycerol saline. Control positive and negative smears were included in each batch.

In positive smears only the one stained with conjugated serum mixed with normal mouse-brain showed specific fluorescence. Fluorescent particles ranging from barely visible to 20μ in diameter were seen. The smaller particles which were unidentifiable as rabies inclusions by Sellers stain were found to be diagnostic. Ring shaped fluorescent bodies with central dark mottling were seen in every positive specimen. Non-specific fluorescence and its prevention or recognition are discussed in detail.

825 brains from a wide variety of species were examined by the above technique and also by Sellers stain and mouse inoculation. The fluorescent antibody technique agreed in every case with the result by mouse inoculation. No false positives were recorded by the fluorescent antibody method. 4 specimens negative by Sellers stain (no Negri bodies seen) were diagnosed by fluorescent antibody and mouse inoculation. 10 specimens in which Negri bodies were reported but which did not infect mice also gave negative results with the fluorescent antibody method.

[See also this *Bulletin*, 1959, v. 56, 1125.] *C. E. Gordon Smith*

Eronat, G., Ari, A. & Okkan, S. [**A Clinical Case of Neuritis due to Rabies Vaccination**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1960, v. 20, No. 2, 276–9. [In Turkish.] English summary.

Among 248,510 persons vaccinated against rabies in Turkey between 1933 and 1959 there were 19 paralytic accidents, with 5 deaths. The vaccine used is prepared from sheep brain with 0·5% phenol.

One case is described in detail: this patient recovered.

The incidence of paralytic accidents is regarded as being low compared with that in many other countries. *H. J. O'D. Burke-Gaffney*

HUYGELEN, C. L'effet de l'inoculation intracérébrale de virus Flury H.E.P. (High Egg Passage) pendant le période d'incubation de la rage des rues chez la souris. [**Effect of the Intracerebral Inoculation of HEP (High Egg Passage) Flury Virus during the Incubation Period of Street Rabies in the Mouse**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 666–71. [22 refs.]

It had already been shown by KOPROWSKI *et al.* [this *Bulletin*, 1954, v. 51, 574 and 1242; *Bact. Proc.*, 1955, 75] that adult mice could be protected by a previous intracerebral inoculation of HEP Flury virus against subsequent challenge with street rabies virus. In experiments now reported the author investigated the effect of an intracerebral inoculation of HEP Flury virus on mice after their infection with street virus, *i.e.* during the incubation period of street rabies. In these experiments the Flury virus used had undergone about 195 serial passages in developing chick embryo, had completely lost its virulence for adult mice, and, on titration in baby mice before use, showed a titre of $10.^{-3.5}$ In all experiments each mouse received intracerebrally 0·03 ml. of a 1 in 10 suspension of chick embryo material infected with the Flury virus. The 2 strains of street virus used were of canine origin and had each undergone a single brain-passage in mice; in all experiments mice received 0·10 ml. of a 1 in 10 brain suspension into the right gastrocnemius muscle.

In the first experiment—one of a preliminary nature—3 groups, each of 6 mice, received street virus intramuscularly; group (a) had, 3 days previously, received HEP Flury virus intracerebrally; group (b) received the 2 inoculations simultaneously; and control group (c) received no Flury virus. In group (a) all animals survived, none having shown any signs of rabies; in group (b), in which 1 had died of trauma, 3 of the 5 remaining mice survived, and of the 2 which died of rabies 1 had paralysis of the hind legs for 12 days; and in group (c) 5 of the 6 died of street rabies—a mortality of 83·3%, as compared with one of 40% in group (b). In the second experiment groups of mice—10 in each group—were first inoculated intramuscularly with street virus and then, after 1, 2, 4, 5 and 6 days, respectively, with HEP Flury virus intracerebrally. The percentage mortality among the groups varied from 0 to 40, as compared with 58 among the controls. In the group which received the Flury virus 2 days after infection, only 1 out of 8 (12%) died of street rabies and among the survivors 2, which had shown transitory paresis of the hind paws, completely recovered after 5–7 days. In the third experiment 160 mice were first inoculated intramuscularly with street virus of a strain different from that used in the 2 previous experiments; groups, each of 18–20 mice, then received HEP Flury virus intracerebrally 1, 2, 3, 4, 5, 6 and 7 days respectively after the street virus inoculation. The mortality percentage among the groups receiving Flury virus 1, 2, 3, 4 and 5 days, respectively, after infection was 21, 25, 33, 37 and 20, as compared with 72 among the controls.

These results, together with observations made by the author during his experimental work, permit the effects of the intracerebral inoculation of HEP Flury virus during the incubation period of street rabies to be summarized as follows. 1. A lowering of the mortality rate, particularly among animals receiving the Flury virus during the first 5 days after infection. 2. A prolongation of the duration of clinical illness. (Several animals, *e.g.*, showed before death symptoms of paralysis for a period of several days; in certain cases the

period of paralysis lasted more than a week and in one case 11 days.) 3. Partial or complete recovery. (4 mice, *e.g.*, completely recovered after having shown paralysis of the hind legs for several days; 6 others survived, but 50 days after the onset of symptoms still showed paralysis in one or both of the hind legs.) *G. Stuart*

i. Constantinesco, N. & Birzu, N. Sur le mécanisme du processus d'autostérilisation et de guérison dans la rage. [**Mechanism of Auto-Sterilization and Cure in Rabies**] *Giorn. di Malattie Infettive e Parassit.* 1960, Sept.–Oct., v. 12, Nos. 9/10, 712–13.

ii. ————, ———— & Micu, I. Recherches sur le mécanisme de l'activité protectrice du sérum antirabique. [**Studies on the Mechanism of Protective Activity of Antirabies Serum**] *Ibid.*, 713–15. [10 refs.]

iii. ————, ————, ————, Zavate, O. & Vasoiu, F. Processus d'autostérilisation dans la rage humaine. [**Process of Autosterilization in Human Rabies**] *Ibid.*, 715–17. [21 refs.]

i. Mice were immunized with one or several courses of 6 injections of Fermi vaccine. They were then inoculated intracerebrally with various doses of fixed virus (Babès) and at intervals the brains of random mice were titrated for virus. Titres in the brains of control mice were consistently 1·6–6·3 log higher than in vaccinated mice and up to 9·5 log higher than in mice given several courses of vaccine.

Mice given antirabies serum 48 hours before intracerebral challenge and 5 minutes after it, were protected against infection with fixed virus by peripheral routes but when inoculated intracerebrally the majority became paralysed. Titres of the brains of such mice did not differ from those of controls. The authors believe therefore that the protective effect of vaccination is due to tissue immunity rather than to circulating antibody.

ii. Hyperimmune antirabies serum capable of neutralizing about 6 log of virus *in vitro* was administered intraperitoneally to mice 24 hours before and at various intervals after fixed virus given also intraperitoneally. 1 ml. of serum protected all and 0·1 ml. half the mice when given 24 hours before virus. 1 ml. and 0·1 ml. given 5 minutes after the virus also protected all. 1 ml. given 2 hours after the virus protected all but the same dose after 4 hours protected only half. Later doses of serum had no effect. When the fixed virus was given intramuscularly and the serum subcutaneously about half the mice were protected by serum given 24 hours before virus but no protection occurred when serum was given 1 hour or later after the virus. When this experiment was repeated with street virus 85% of the mice were protected by serum given 1 hour after the virus and 41% by serum 24 hours after. The longer incubation period of street virus appears to permit the serum to take effect when administered after the virus. This was shown by the fact that the mean incubation periods in the mice given fixed virus intramuscularly varied only from 4·1–5·5 days with serum given subcutaneously from 1 hour to 4 days after, compared with 4·2 days for controls. With mice similarly given street virus the mean incubation period of the controls was 11·6 days compared with 25 days when serum was given after 1 hour, and 17·1–18·2 days when it was given 1–4 days after.

iii. The brains of 6 patients who had died of rabies were titrated by intracerebral inoculation of mice. 3 had not been treated, had incubation periods of 17–52 days and their illness lasted 4 days. Their brains titred 4·5, 4·3 and 4·3 log LD50. After one passage in mice the respective titres were not significantly changed (5·3, 4·5, 4·9 log). The other 3 had been treated, had incubation periods of 16 days, 20 days and 7 years [?], and their illnesses lasted 5 days, 6 days and 22 days respectively. The titres of the brains were 1·5, 2·5 and 2·5 log but after one passage in mice were 4·3, 5·2 and 5·2 log respectively. This phenomenon appears similar to the experimental results in the first of these 3 papers. *C. E. Gordon Smith*

PLAGUE

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, rodent hosts, transmission, pathology, diagnosis, clinical findings, treatment, control.

BRYGOO, E. R. & RAJENISON, S. Puces et rats d'un village de l'Itasy en zone d'endémie pesteuse. [**Fleas and Rats in a Village in the Itasy Region, Madagascar, in an Endemic Area of Plague**] *Arch. Inst. Pasteur. de Madagascar*. 1960, v. 28, 109–24.

In a village in Madagascar, where human plague is still seen, the nature and habits of the rodent and flea populations, and their contacts with man, were investigated over a whole year. Rat traps were placed in the village and up to 500 m. outside its periphery; of 575 small mammals captured, 572 were *Rattus rattus*. Recaptures after release indicated that rats do not travel far. Only 3 were recaptured more than 100 m. from their first capture. The villagers alleged that there are increases in the rodent population in March-April and June-October, and that rodent mortality is greatest in August-September. In the experiment it was noted that young were trapped most frequently in April and December, though reproduction continues throughout the year. Of fleas taken from rats, in the fields *Synopsyllus fonquerniei* was much the commonest, in granaries *Leptopsylla segnis*, and in habitations *Echidnophaga gallinacea*, but *Xenopsylla cheopis* also was common. Free-living fleas were captured by means of traps and the following species were identified: *Pulex irritans* (224 out of 249 caught), *Ctenocephalides canis, C. felis, Tunga penetrans, Echidnophaga gallinacea* and a single *Xenopsylla cheopis*.

The village was sprayed with DDT. 4 days later, as a part of a general programme, it was also sprayed—walls and floors, houses, granaries and pig-sties—with a dieldrin-malathion mixture. The flea index among "field" rats was unaffected but that among the "house" rats was markedly diminished for 3 months. The effect had disappeared after 7 months.

While the danger of making too sweeping conclusions is admitted, it does appear that *Rattus rattus* is the exclusive local danger as regards plague, and that insecticides do not affect fleas among "field rats" and are therefore of limited use in controlling plague. Nevertheless, no local flea species is resistant to insecticides, and the raised murine mortality in August-September, followed

by a markedly increased flea index in October, is an indication for the use of insecticides in the July-September period. It was also noted that the villagers lacked the most elementary knowledge of rat control, and that education in this respect must be an essential part of any campaign against endemic plague.

B. B. Waddy

HUDSON, B. W. & QUAN, S. F. **Use of Fluorescent Antibody Technique for detection of *Pasteurella pestis* in Rodents.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 599–600.

This correspondence draws attention to the recent demonstration by WINTER *et al.* [this *Bulletin*, 1960, v. 57, 120] that plague bacilli can be rapidly identified in the tissues of experimentally infected laboratory white mice by means of the fluorescent antibody technique and then goes on to show that similarly infected laboratory and field-trapped wild rodents were also suitable for fluorescent antibody examination although the results were somewhat variable. Nevertheless it is suggested that the technique might be profitably employed in field studies of the ecology of sylvatic plague.

[Confirmation of the value of this technique as applied to field studies of plague-infected animals found dead has already been published by KARTMAN (*ibid.*, 1961, v. 58, 313) in connexion with his studies on the part played by wild rabbits in the epidemiology of sylvatic plague. It would appear that the two investigations are associated since both are reported from the San Francisco Field Station, Communicable Disease Center, U.S. Department of Health, Education and Welfare.] *H. J. Bensted*

SMITH, H.; KEPPIE, J.; COCKING, E. C.; WITT, K. **The Chemical Basis of the Virulence of *Pasteurella pestis*. I. The Isolation and the Aggressive Properties of *Past. pestis* and its Products from Infected Guinea-Pigs** [SMITH, KEPPIE, COCKING & WITT]. *Brit. J. Exper. Path.* 1960, Oct., v. 41, No. 5, 452–9, 1 fig. [24 refs.] **II. The Toxicity for Guinea-Pigs and Mice of Products of *Past. pestis*** [COCKING, KEPPIE, WITT & SMITH]. *Ibid.*, 460–71, 1 fig. [18 refs.] **III. An Immunogenic Product obtained from *Past. pestis* which protects both Guinea-Pigs and Mice** [KEPPIE, COCKING, WITT & SMITH]. *Ibid.* 1960, Dec., v. 41, No. 6, 577–85, 1 fig. on pl. [14 refs.]

These papers describe attempts to identify the compounds responsible for the virulence and immunogenicity of *Pasteurella pestis*. The approach is novel in that the fractionation of *P. pestis* was done on cultures obtained directly from guineapigs dying from experimental plague and that the basis for chemical fractionation has been biological assays for aggressins, toxins and immunogens in both guineapigs and mice. Although both animals are equally susceptible to plague infections the so-called toxin is lethal for mice but not for guineapigs. It was therefore considered that the examination of material from guineapigs dying from plague, which would contain both the organisms and their extracellular products, might yield information of value.

I. The first paper describes the procedures adopted for the collection and treatment of the plague cultures: 400 large guineapigs were each given 3·5 ×

10^8 organisms, both intrapulmonarily and intraperitoneally, of a culture of the virulent strain L37 of *P. pestis* grown at 28°C. for 32 hours. Death occurred in 36–50 hours when heparinized saline was injected into the thorax and peritoneum and a little later each animal was slit open along the ventral line and the exudate-suspension allowed to drain out. Differential centrifugation was used for purification of the suspension of *P. pestis* which was then subjected to extraction with ultrasonic waves. After centrifugation the supernatant, which was the ultrasonic extract, represented about 70% by weight of each organism. The residue consisted predominantly of cell wall material. The total yield from the 400 guineapigs was about 6 gm. *P. pestis*.

The material obtained from the organisms grown *in vivo* possessed virulence-enhancing activity and also anti-phagocytic activity against both guineapig and mouse cells. Examination of the precipitation lines showed that the ultrasonic extract contained Fraction 1 (antigen 3) and the precipitinogens V and W. Two extra lines, X and Y, were found in the whole organisms of virulent cultures.

II. Products prepared from a number of organisms, which was less than the number found in guineapigs dying of plague, were found to be fatal to healthy animals. Ultrasonic disintegration of cultures grown *in vivo* yielded products which were toxic to both guineapigs and mice; the toxicity was divided between the soluble extract and the residue. For mice, the major toxicity appeared to be in the soluble extract, whereas for the guineapig the toxicity was due to two components, unequally divided between the cell wall material—the residue—and the soluble extract. These components have been separated from the extract but not yet defined. Products of the same nature were later obtained from cultures of *P. pestis* grown *in vitro*.

The toxic deaths were accompanied by the same clinical signs of shock as were noted in the animals injected with untreated cultures of living, virulent organisms, but the degree of oedema noted was not sufficiently large to warrant the assumption that it was the primary cause of shock.

III. The residue obtained after ultrasonic disintegration of *in vivo* cultures in guineapigs was found to contain an immunogenic agent which protected guineapigs, as well as mice, against a virulent challenge of *P. pestis*. The substance concerned was mainly bacterial cell wall, which comprised lipid, carbohydrate and protein. The residue also immunized mice, but not so efficiently as the extract, which was not effective for guineapigs.

The estimated Fraction 1 content of the soluble extract and the residue after ultrasonic disintegration could not explain the different immunizing properties of the two products, but it is suggested that the residue contains a relatively large immunogenic fragment of native cell wall, or envelope-complex, which is probably the most suitable immunogen for all animal species. This product which was first recognized in *P. pestis* grown *in vivo* was later recognized in certain cultures grown *in vitro*.

It is suggested that the observations recorded here indicate that a non-toxic, sterile vaccine of suitable immunogenicity could be prepared from *P. pestis* which would be effective in immunizing guineapigs, mice and possibly man against natural plague infections. *H. J. Bensted*

CHOLERA

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

GHOSH, D. K., HALDAR, D., GHOSH, B. K. & CHATTERJEE, A. N. **Pentose Phosphate Cycle in** *Vibrio cholerae*. *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Aug., v. 20, No. 8, 221–6, 3 figs. [12 refs.]

HOWARD, Mary B. & LANKFORD, C. E. **Minimum Nutritional Requirements for Mucinase Synthesis by** *Vibrio cholerae*. *Texas Reports on Biol. & Med.* 1960, v. 18, No. 4, 612–19. [15 refs.]

PANT, K. D.; SHRIVASTAVA, D. L.; MISRA, S. B. **Studies in Immunochemistry of** *Vibrio cholerae*. **Part II. Preparation of Polysaccharides from Growth on Agar** [PANT & SHRIVASTAVA]. *Indian J. Med. Res.* 1960, Nov., v. 48, No. 6, 677–82, 1 fig. & 1 graph. [14 refs.] **Part III. Characterization of Polysaccharides isolated from Broth Cultures** [MISRA & SHRIVASTAVA]. *Ibid.*, 683–91, 1 fig. & 1 graph. [20 refs.]

MORGAN, F. M., FELSENFELD, O., RODVATANAKUL, B., BUSPAVANICH, S., BANDHUMEDHA, B. & CHOWVANASAI, A. **A Study of Patients with Mild Cholera in Bangkok, Thailand, Spring, 1959.** *Amer. J. Hyg.* 1960, Sept., v. 72, No. 2, 250–60. [16 refs.]

In the latter part of 1958 an outbreak of cholera, which assumed epidemic proportions, occurred in Bangkok. It extended into the early months of 1959, but by April of that year only a few cases of classical cholera were being reported. There were, however, large numbers of low-grade diarrhoeas of questionable aetiology and it is this group of cases on which the present study was based. The group consisted of 231 consecutive patients in whom diarrhoea was associated with nausea, vomiting and intestinal cramps or cases where there was diarrhoea only.

A total of 155 patients were found to be excreting *Vibrio cholerae,* sub-type Ogawa, either as the only vibrio or accompanied by non-agglutinating vibrios (NAG); 23 shigellae and 25 salmonellae were also isolated from the group, either alone or in conjunction with one of the other organisms mentioned. There were 36 patients from whom a pathogenic organism was not recovered; it is not quite clear from the records whether these include the relatively few patients who were excreting only non-agglutinating vibrios, but it is of interest to note that the authors specifically indicate that they do not wish to discuss, with regard to the present study, the significance of these NAG vibrios. Apart from 6 patients in this group who suffered from severe cholera it was not possible clinically to differentiate the true mild cholera case from the salmonellosis or shigellosis cases or indeed from the bacteriologically negative case.

Although Hikojima and Inaba sub-types had been isolated in Bangkok before, and subsequent to, these studies all the strains reported here were *V. cholerae,* Ogawa. [See also SEATO, Cholera Research Laboratory Report, this *Bulletin,* 1961, v. 58, 194.] *H. J. Bensted*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

WYKOFF, D. E. & RITCHIE, L. S. **Intestinal Protozoa in Family Groups of Four Japanese Villages.** *U.S. Armed Forces Med. J.* 1960, Oct., v. 11, No. 10, 1106–16, 1 fig. [13 refs.]

The observations here recorded were made in 4 rural villages situated in the Kofu Valley, Honshu, Japan. An average of 4·94 stools passed over a 10-day period were examined from each of 1,037 persons belonging to 172 families.

Only 2 of the families were found completely free of protozoa, the incidence by family for *Entamoeba histolytica, Entamoeba coli* and *Endolimax nana* being 69, 95 and 88% respectively.

The epidemiological picture embraced a number of factors that appeared normal for rural Japan—sanitation, personal hygiene, prevalence of flies, practices of handling night soil and general living habits. These factors were common to all rural villages in Japan, but the water supply was a variable related to incidence. It is considered that where incidence is high, as in the present study, water may be the predominant means of transmission, whereas other factors may be relatively more important in areas of moderate or low endemicity.

No seasonal variation in incidence was noted; size of family and resulting overcrowding did not appear to be an epidemiological feature of any importance. The results are set out in a figure and 5 tables, and discussed.

G. Covell

GÓMEZ MALARET, S., LOZANO, D. V., SUCRE, A., LATUFF, H., SIRVENT, F., PANTOJA, E., REYES, T. & ARREAZA, R. Estado actual de la amibiasis en el Hospital de Niños " J.M. de los Rios ". [**Current Position of Amoebiasis in the Children's Hospital in Caracas, Venezuela**] *Archivos Venezolanos Puericult. y Pediat.* 1960, Jan.–June, v. 23, Nos. 75/76, 19–50, 2 graphs. [60 refs.]

During 1958, 241 autopsies were carried out at the Children's Hospital, Caracas, and in 15 the cause of death was amoebiasis. From June to December of that year, 3,243 children were admitted and 71 (2·2%) showed evidence of proved amoebiasis, mostly severe, with a mortality of 18·3%. Among 3,559 out-patients, routine stool examinations showed that 157 contained trophozoites

of *Entamoeba histolytica* but when special examinations were made in fresh specimens, the percentage positive reached as high as 43·7.

The findings suggested that the disease was on the increase and the present paper describes a study of the 71 in-patients with amoebiasis. Results are given in great detail in tables and figures. The data include epidemiological features, clinical and pathological features and treatment.

A socio-economic study was made of the background of 48 children and related to such factors as housing, water, sanitation and the presence of flies. Findings are listed and it is evident that poor conditions were present in some 65% to 83% of cases. Similar findings were obtained in regard to malnutrition and in every case multiple parasitism was present. More than half the cases were in children aged 2 to 6 years and 16·9% were in those under 2 years. The clinical forms are discussed in detail. 57 were of the intestinal form, with recovery, and 4 were fatal cases of the same form. 9 had liver abscesses and 1 had an abscess of the liver and lung. There were 9 deaths among the extra-intestinal forms. Histories of the 4 fatal cases of intestinal amoebiases are given and details of full clinical and laboratory findings are listed for the 10 extra-intestinal cases. A battery of anti-amoebic drugs was tried, together with antibiotics. The authors favour emetine, where the children's condition allows of it and consider oxytetracycline to be the best of the antibiotics.

The distribution of the lesions in the liver and intestines is given.

The results are discussed at length. The authors consider that the problem is an important public-health one. They note the frequency of liver abscess (14%) in children.

They advocate improvement of hygiene and nutrition and treatment of both intestinal and extra-intestinal lesions as the best form of prophylaxis of this "social disease". *H. J. O'D. Burke-Gaffney*

KUNERT, H. Über das Auftreten besonderer Wuchsformen in Kulturen von *Entamoeba histolytica*. [**Occurrence of Special Growth Forms in Cultures of** *Entamoeba histolytica*] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1960, v. 11, No. 1, 6–12, 8 figs.

The author describes the appearance of unusual forms of *Entamoeba histolytica* in a strain cultivated in a fluid medium composed of 1·25 cc. of a filtrate of fresh human faeces autoclaved for 30 minutes, to which 0·75 cc. of horse serum and some rice starch were added. The protein content of the medium varied from 3·07 to 3·87%, with *p*H from 6·9 to 7·8.

This strain was isolated from a patient in 1958 and cultivated for 73 generations in Dobell's media, after which it was transferred to the above (FS) medium. From the 14th subculture onwards there began to appear in cultures abnormal amoeboid forms, some rounded measuring 80 × 120μ, others, giant plasmodial bodies forming a network and measuring 500–1000 × 400–700μ, in addition to scanty normal amoebae. The giant forms were multinucleate and produced pseudopodia. When transferred to Dobell's media the giant forms gradually disappeared and were replaced by normal amoebae. It is noted that other strains cultivated in the FS medium grew normally. As the giant forms of the strain in question did not appear in medium containing freshly prepared faecal filtrate with a high protein content (3·87%), but only in old media in

which the protein content had fallen to 2·93%, it is thought that the abnormal growth of *E. histolytica* might have been due to the action of the products of break-up of protein, *viz.* the amino-acids, present in the medium.

The appearance of the giant amoebic plasmodia is illustrated by a number of photomicrographs. *C. A. Hoare*

SCHNEIDER, J. Essai de classification des manifestations cliniques de l'amibiase en fonction de l'origine de la contamination chez 2.111 malades observés à Paris, de 1948 à 1960. [**Attempt to Classify the Clinical Features of Amoebiasis in Relation to the Origin of Infection in 2,111 Patients seen in Paris between 1948 and 1960**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 671–90, 2 graphs.

Over a period of 12 years prior to 1960 the author in Paris dealt with 2,111 patients with amoebiasis diagnosed by recovery of the parasite from the stools. 1,475 of the patients were men, 518 women, and 118 children; of the last, 16 were under 5 years of age and the remainder under 15 years. This paper is an analysis of the probable geographical origins of infection of the various patients, and of the pathogenicity or non-pathogenicity of the infections acquired in the various geographical areas.

The patients have been classified into those who probably contracted their infections in countries where amoebic dysentery is recognized as endemic, and those found to be infected though living in areas where it is not considered to be endemic among the indigenous inhabitants (" autochthonous amoebiasis "). The regions considered to be endemic areas from which the patients came were the Far East (Indo-China, and elsewhere), Central Africa (including Madagascar), North Africa (Algeria, Morocco, and Tunisia), tropical America (continental, and Antilles), and the Near East (and Eastern Europe). The data are set out in some detail in tables and in block graphs; these should be consulted in the original by those interested.

The author draws these conclusions from his investigation. Progressive pathogenic, clinical manifestations of amoebiasis are encountered in Indo-China (particularly among those who acquired their infections during military operations), in Morocco, and, to a lesser degree, in Algeria; and also among those incarcerated in the prison camps in Europe between 1939 and 1945. In these areas, with the exception of Morocco, the essential conditions were comparable, and the aetiological factors were those of what he refers to as " war amoebiasis ".

Amoebiasis in patients who have not resided in countries of recognized amoebic dysentery endemicity is rarely symptomatic, although among such patients 3 examples of amoebic liver-abscess formation have in fact been recorded. The author is impressed by his own experience that the house and family contacts of patients with asymptomatic amoebiasis commonly are affected likewise, and that when the diagnosed patient is treated reappearance of the parasites in the stool is not due to failure of the treatment but to reinfection with the parasite from his contacts.

Patients infected in North Africa vary in their reactions to the infection according to their origin. Among Europeans the pathological manifestations of the infection often are severe; but the inhabitant of the region suffers little

from it or remains a healthy carrier of the parasite. The explanation may well lie in the alterations in the intestinal flora which are associated with changes in residence and conditions of life and diet; this especially applies to the young soldier on active service who necessarily lives under poor conditions of sanitation and who suffers severely from amoebic dysentery infection—thereby justifying the author's term "war amoebiasis".

[This paper should be consulted in the original by those interested.]

A. R. D. Adams

HAMILTON, I. & LUTWYCHE, Ursula. **Dyspnoea due to Subclinical Amoebiasis.** [Correspondence.] *Lancet*. 1960, Dec. 17, 1352.

In January 1959, a young man of 23, working in Harlow, Essex, complained of tightness of the chest, breathlessness and wheezing of 3 months' duration. The attacks lasted for about an hour and were not relieved by antispasmodic drugs. There was no history of asthma or other illness, other than a mild attack of dysentery during service with the Forces in Egypt in 1954–55.

The patient's general condition was good and physical and laboratory examinations showed no abnormalities of significance, until the stools were examined because of the history. This examination revealed the presence of large numbers of cysts of *Entamoeba histolytica*. Specific treatment resulted in considerable improvement in the patient's condition, the respiratory symptoms eased quickly and within 2 months the patient was free from symptoms and has remained so for a year.

The correspondents record this case as an example of respiratory symptoms due to latent amoebiasis in a young man after National Service in Egypt, so that other practitioners in Britain might keep such a condition in mind.

H. J. O'D. Burke-Gaffney

DELANOE, G. Un cas de péricardite purulente amibienne. [**A Case of Purulent Amoebic Pericarditis**] *Maroc Méd*. 1960, Oct., v. 39, No. 425, 1072–3, 2 figs.

See also this *Bulletin*, 1956, v. 53, 1426.

ZIPRKOWSKI, L., KRAKOWSKI, A. & SCHEWACH-MILLET, M. [**Amoebiasis of the Skin**] *Harefuah*. Jerusalem. 1960, Dec. 1, v. 59, No. 11 [in Hebrew 339. English summary 339].

The English summary appended to the paper is as follows:—

"The presence of amebic ulcers in the skin of the ano-genital region is described in a patient suffering from clinically unrecognised amebic colitis. The patient was referred to us with the diagnosis of primary syphilis. The true etiological factor, *Entamoeba histolytica* was demonstrated in a smear taken from an ulcer. Treatment with emetine resulted in a dramatic recovery.

"The case belongs to type 2 of the cited classifications: amebiasis of skin due to prolonged contact with infected excretions of the ano-genital region. The importance of looking for amebae in every case of ano-genital ulcers, especially in tropical and subtropical countries like Israel, is stressed."

LIESKE, H., HAAGE, H. & BUCK, A. A. Zur röntgenologischen Kontrastmittel-Darstellung von Amöben-Leberabszessen. [**Radiological Demonstration of Amoebic Abscesses of the Liver with the Use of a Contrast Medium**] Reprinted from *Acta Hepato-Splenologica*. Stuttgart. 1960, June, v. 7, No. 3, 141–54, 11 figs. [17 refs.]

This work was undertaken in the German Red Cross hospital in Pusan, South Korea (period not stated). The results of X-ray demonstration of liver abscess in 14 cases by the use of Perabrodil M as a contrast medium are recorded. This contrast medium is easily applicable and is quickly absorbed by the liver tissues and it is, moreover, well tolerated. It is therefore the method of choice.

To avoid any allergic reactions an intradermal test is undertaken. The pus within the abscess is drained off with a long cannula. The Perabrodil is then injected in a 45% solution in quantities from 5–60 ml., depending on the size of the abscess cavity; air can be added, and specific drugs such as resochin [chloroquine]. By the aid of this contrast medium the localization and the size of the abscess cavities can easily be determined, and so it can be decided whether conservative therapy or surgical intervention is necessary. By this method also it is possible to judge the shrinkage of the abscess cavity by specific therapy or by drainage.

The application of this contrast medium is illustrated in 4 cases by radiograms which show, quite convincingly, the air space and horizontal fluid level. Details of all 14 cases are tabulated. *Philip Manson-Bahr*

SCHAPIRO, M. M. **The Therapeutic Efficiency of a New Amoebicide among Prison Inmates.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 564–73, 4 charts.

The drug is diloxanide (Entamide, dichlor-acet-hydroxy-methylanilide) [this *Bulletin*, 1961, v. 58, 65] and it is referred to by the author as DHM. The overall incidence of *Entamoeba histolytica* infection among the inmates of the Central Penitentiary in Honduras is very high (61·1%). The overcrowding and absence of sanitary provisions, both personal and communal, in this prison together with the methods for excrement collection and disposal, as described, are almost unbelievable. For this study 135 inmates were selected and relegated by serial allocation into one or other of 4 groups. The selection was determined by microscopical proof of a current intestinal *E. histolytica* infection together with absence of a history of clinical manifestations of its presence at least for the preceding 6 months. Each patient was treated orally with 2 tablets thrice daily over a period of 10 days. These 2 tablets for the first group contained DHM (900 mgm.) alone; for the second group they contained DHM (900 mgm.) + chloroquine diphosphate (100 mgm.); for the third group DHM (900 mgm.) + chloroquine diphosphate (100 mgm.) + tetracycline (20 mgm.); and for the fourth group diiodohydroxyquinoline (900 mgm.) + chloroquine diphosphate (100 mgm.).

The results of the various treatments, as judged by stool examinations on the last 2 days of treatment, on the day following it, weekly for a month, and monthly thereafter to the end of the sixth month, are set out in a number of

graphs and attached tables. From these data the author concludes that the most effective of the 4 courses of treatment used were those given to the second and third groups of patients (*i.e.* DHM + chloroquine and DHM + chloroquine + tetracycline), and that that given to the fourth group was the least effective.

As there seemed to be some connexion between the effect of the treatment and the stage of the parasite being passed in the stools at the time of treatment, this matter was looked into. Further data relating to this are presented in graphic form. The author concludes from these data that when amoebae alone, or cysts alone, are being passed treatment is more effective than when both are being passed concurrently.

Some 80 patients with stools free from *E. histolytica*, inhabiting the same cells as those infected, were then divided into groups. These variously were given one or other of the two drug formulations mentioned above as the most effective treatment, or they were given diiodohydroxyquinoline alone or else thiamine hydrochloride alone as a control treatment. The daily dosage was that previously given but it was continued over 15 days. This prophylactic experiment, in the author's view, shows the first 2 dosage schedules to be equally effective as prophylactics, but the last had no effect [the chart indicates infection rates steadily rising from zero at the end of treatment up to 80 to 100% in each case by the eighth week]. He suggests that DHM, in view of the "excellent results in the present study", is worthy of further investigation and that combination with other drugs will enhance its activity.

[The abstracter has not been able to correlate the data set out in some of the graphs and tables; furthermore it seems to him that conclusions drawn from figures derived from such small groups of patients may not be so convincing as the author finds them.] *A. R. D. Adams*

Donckaster, R. & Donoso, A. Amibiasis intestinal crónica. Ensayo terapéutico con tetraciclina-triacetiloleandomicina. [**Chronic Intestinal Amoebiasis. Therapeutic Assay with Tetracycline-Triacetyloleandomycin**] *Bol. Chileno de Parasit.* 1960, Oct.–Dec., v. 15, No. 4, 78–80. [18 refs.]

The English summary appended to the paper is as follows:—

"1.—37 patients with chronic intestinal amebiasis were treated with a combination of antibiotics (Sigmamycin) which contains 167 mgrs. of tetracycline and 83 mgrs. of triacetyloleandomycin. Two capsules of Sigmamycin, three times a day were given for ten days.

"2.—Stool examinations were done with a combination of Telemann and Polyvinyl alcohol techniques at 10, 30 and 90 days after treatment, in order to estimate its success.

"3.—More than 80% of the patients appeared free from *E. histolytica* in the three series. The efficiency evaluated at 90 days after completion of treatment was the best obtained with antiamebic drugs so far tested in our out-patient service.

"4.—Intolerance to the drug was observed in 60% of the patients, but symptoms disappeared when the treatment was completed. Pruritus ani showed the highest incidence (30%).

" 5.—The authors believe Sigmamycin is an adequate drug for the treatment of chronic intestinal amebiasis."

EL SHEIKH, A. **Paromomycin in the Treatment of Intestinal Amebiasis.** *Antibiotic Med.* New York. 1960, Nov., v. 7, No. 11, 681–4.

62 patients in Cairo with acute amoebic dysentery, diagnosed microscopically, were given paromomycin orally at a daily dosage of 25 mgm./kgm. body weight (in divided doses) for 5 days. All of them enjoyed symptomatic relief within the period of treatment, usually by the third day; all but 8 of these patients appeared to be sterilized of the infection by the treatment, as judged by weekly stool examinations for another 3 months and a couple of sigmoidoscopic examinations. The patients not cured were re-treated with a double dose of the drug and 5 of them were successfully cured by this.

28 patients (23 men and 5 women) with chronic symptomatic intestinal amoebiasis were similarly treated; 17 had symptomatic relief, but only 6 patients became stool-negative; in another 3 the parasites reappeared in the stools after temporary clearance.

Paromomycin therefore was curative in acute amoebic dysentery, but less than 50% effective in the chronic disease. It was well tolerated.

A. R. D. Adams

DE CARNERI, I. & ALMIRANTE, L. **On the Reliability of the *in vitro* and *in vivo* Determinations for testing Anti-Amoebic Compounds.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 598–9.

The authors are concerned with difference in results obtained during tests for anti-amoebic activity by *in vitro* and *in vivo* methods which is in part bound up with the antibacterial activity of the substances under test. Details are given in the case of chlorophenoxamide derivatives, some of which are active *in vitro*, others *in vivo* [this *Bulletin*, 1958, v. 55, 1011, 1013]. Chloroquine on the other hand, which shows little activity *in vitro*, is active *in vivo*. In another series of dichloroacetamide derivatives, in which a piperazine nucleus is present, activity against bacteria is low but high against trophozoites of *Entamoeba histolytica in vitro*, while *in vivo* activity is low whether given *per os* or *per anum*. The authors conclude [and all who have worked in the field would agree] that *in vitro* anti-amoebic screening must be supplemented by *in vivo* tests.

J. D. Fulton

BARROW, J. H., Jr. & STOCKTON, J. J. **The Influences of Temperature on the Host-Parasite Relationships of Several Species of Snakes infected with *Entamoeba invadens*.** *J. Protozoology.* Utica. 1960, Nov., v. 7, No. 4, 377–83. [14 refs.]

RELAPSING FEVER AND OTHER SPIROCHAETOSES

LANZO, A. & TRESCA, G. La novobiocina nella cura delle febbre ricorrente. **[The Treatment of Relapsing Fever by Novobiocin]** *Giorn. di Malattie Infettive e Parassit.* 1960, May–June, v. 12, Nos. 5/6, 268–9.

20 female patients, apparently in Asmara, Eritrea, between 7 and 36 years old, suffering from louse-borne relapsing fever in whom the diagnosis had been confirmed by thick blood drop examinations were treated with novobiocin intramuscularly. Dosage was in units of 250 mgm. and varied according to the weight of the patient and the seriousness of the infection. Interval between doses was either 6, 8, or 10 hours on the same criteria. The total dosage varied from 250 to 1,000 mgm. Improvement was dramatic, clinical cure and the disappearance of the treponemes from the blood being attained in 12 to 40 hours. The drug was well tolerated. Only 40% of the patients could be followed up for 30 to 35 days but these showed no recurrence. *E. Agius*

LEPROSY

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

TAKIGAWA, K. **[An Epidemiological Study of Leprosy in Japan]** *Igaku Kenkyu.* Fukuoka. 1959, May, v. 29, No. 5, 1427–37. [20 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"1. Though at the beginning of this century, the number of deaths from leprosy amounted to above two thousand, or 4·8 per 100,000 persons, it declined gradually, only 13 in 1957, or 0·01 per 100,000. But these figures do not tell the actual decline rate of leprosy mortality, because in recent years most of deaths occurring in the leprosariums have been reported as due to some direct causes of death other than leprosy, in spite of the fact that number of deaths in leprosariums has not declined in recent years.

"2. Male deaths are more than twice the number of female deaths, and in the Meijiera the deaths occurred most frequently at ages 20–39, in recent years the deaths are most frequent at ages 30–49.

"3. The number of lepers reported was annually 600–780 for 1947–1950, since 1951 it has declined to 280–490. It is relatively more numerous in the south-western regions than in the north-eastern parts of the country.

"4. It is a remarkable fact that number of cases reported in children under 10 years of age has markedly declined since 1953.

"5. The number of lepers living in the home amounted to 6681 in 1930–1933, but it decreased to 1223 in 1955. On the contrary, the number of cases hospitalized increased remarkably from 1737 cases in 1925 to 10,319 in 1955.

"6. The total number of lepers decreased gradually from 30,393 in 1904 to about 15,000 in 1955. Most of them are adults above 20 years of age.

"7. Though the number is declining, it must be noticed that new cases are still occurring."

CARRANZA ANAYA, A. Estado actual de la lepra en El Salvador, C.A. [**The Present State of Leprosy in Salvador (Central America)**] *Bol. Soc. Cubana de Dermat. y Sifil.* 1960, June–Sept., v. 17, Nos. 2/3, 84–91. [18 refs.]

The fact that within one year 50 new cases of leprosy have been discovered is explained by the fact that 5 journeys of investigation were made to different parts in the centre of the country. Up to September 1959 there were 178 known cases of leprosy in the Republic. These are classified according to the Departments of the Republic to which they belong, and by sex, type of disease and age. Leprosy has been found in 11 of the 14 Departments, Chalatenango being the Department with most (82). Of the 178 known patients 95 have the lepromatous form.

The population of infection-spreading areas has been inoculated with BCG. Doctors are familiarizing themselves with the signs of leprosy. Most of the patients are being treated as out-patients under medical supervision and control. It is considered likely that there are some 400 more cases besides those registered at present. *Ernest Muir*

PARLETT, R. C. **A Modification of the Oakley Tube Method of the Agar Double-Diffusion Precipitation Test for Mycobacterial Antibodies.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 300–304.

TAYLOR, C. E., HANKS, J. H., MOSES, H., MITTAL, M. C. & KANT, L. **The Antigenic Components of Lepromin as assayed in Guinea-Pigs.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 284–99, 6 figs. [27 refs.]

This is a study of the immunological basis of the lepromin reaction, trials being made of relative sensitization of guineapigs by injections of various antigens. In the first series of experiments 5 groups of 6 to 10 guineapigs were inoculated with 1 of 3 antigens: Wade lepromin (2 groups), normal human skin, and living BCG; and (as a control) one group was left uninjected. In the second series there were 6 groups each of 18 guineapigs injected as follows: Wade lepromin, killed BCG, normal human spleen, BCG plus spleen, phenolized guineapig serum, and (as a control) dilute phenol.

The results are given in a series of graphs. They show that the autoclaving of human tissue does not destroy its antigenicity, and that heated proteins are antigenic in the species of origin. They also show that there is enhanced response to both the tissue and the bacterial contents after sensitization with Mitsuda-Wade antigen, but that the degree of immune response is less than that induced by autoclaved BCG with or without tissue components. The authors therefore consider that it is necessary to separate *Mycobacterium leprae* from tissue components in preparing skin-test reagents for epidemiological investigations, so as to be able "to determine the relative usefulness of soluble antigens and intact bacilli for detecting in the individual: (*a*) prior sensitization, or (*b*) capacity for enhancement of immune response".

Ernest Muir

MONTESTRUC, E & DESPIERRES, G. La réaction de Mitsuda et le rôle du B.C.G. dans la positivité de cette réaction en milieu indemne de lèpre. **[The Mitsuda Reaction and the Role of BCG in the Positivity of that Reaction in an Area free from Leprosy]** *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 630–34.

The authors contest the assertion that when the Mitsuda reaction is converted to positive after vaccination with BCG the conversion is caused by the original injection of lepromin and not by the BCG. An enquiry was carried out at Lyon which is free from leprosy; 112 subjects were chosen, some of them children of 6 to 8 years and others being adults of 18 to 25. All were negative to an intradermal injection of 50 TU tuberculin. In 70 out of the 112 the Mitsuda reaction was tested by intradermal injection of lepromin, and all of the 70 were negative except 9 who gave doubtful reactions. The 112 subjects were then vaccinated with BCG by means of scarification; and 8 or 9 weeks later the Mitsuda reaction was performed and showed that of the 70 who had been previously tested 53 had become Mitsuda-positive and 13 were doubtful. The authors assume that the 42 other subjects whose Mitsuda reaction was not originally tested would have given similar negative results to the 70 who were tested. After BCG vaccination the 42 showed 83% of Mitsuda positives compared with 75·7% among the 70 who were twice Mitsuda-tested. The role of BCG in rendering Mitsuda positive is therefore undeniable.

It was also found that of 12 patients in this leprosy-free area suffering from pulmonary tuberculosis 83·6% gave positive lepromin reactions, while in 11 adults giving a negative tuberculin reaction after BCG vaccination 4 were 1-plus Mitsuda positive. It is therefore confirmed that after vaccination with BCG there is no concord between the intensity of the tuberculin reaction and of the Mitsuda reaction which results. *Ernest Muir*

ROSEMBERG, J., DE SOUZA CAMPOS, N., AUN, J. N. & DA ROCHA PASSOS, M. C., Jr. **Immunobiologic Relation between Tuberculosis and Leprosy. X. Comparative Study of the Results of the Lepromin Test in Subjects submitted to Serial Injections of Mitsuda's Antigen and to Oral BCG Vaccination.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 271–83, 10 figs. [11 refs.]

An objection has been raised that conversion to Mitsuda negativity after BCG vaccination is due to the lepromin antigen and not to the BCG. This paper is an answer to this objection.

Three groups of children of parents with leprosy were chosen. Group A consisted of 21 unvaccinated children who were given 4 lepromin tests at intervals of 3 months. After the 4th test 9 were positive (only 1 necrotic). Then after BCG vaccination 7 of the 12 negative patients became positive. In Group B, 20 children were given BCG 0·10 to 0·20 gm. orally (according to age) thrice at weekly intervals. A lepromin test 9 months later showed 17 (necrotic) Mitsuda positives. After another course of BCG 2 of the 3 negatives became strongly positive (necrotic). Group C consisting of 20

children acted as controls. They were tested with lepromin 9 months after the experiment began, and all were completely negative.

It is concluded that "The orally-administered BCG is able to cause prompt mass conversion of the Mitsuda reactivity, whereas the positivizing effect of repeated lepromin injections is much less frequent, and is slower and weaker". It was noted also that Group C was entirely negative to 1 in 10 Mantoux, while in Group B 14 of the 17 Mitsuda positives were found tuberculin positive.

[For earlier parts, see this *Bulletin*, 1953, v. 50, 420.] *Ernest Muir*

Ross, Hilary. **Immunochemical Determination of Orosomucoid in the Blood Serum of Leprosy Patients.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 267–70.

Orosomucoid is an acid glycoprotein, a major component of seromucoid fractions of serum which increase significantly in a number of diseases. Using the immunochemical method for estimation of specific proteins, and particularly antichick orosomucoid antiserum, the author made estimations of orosomucoid levels in 100 leprosy patients and 17 normal controls. Elevations of serum orosomucoid above normal were found in 57 out of 91 lepromatous patients, 45 of whom were bacteriologically positive and 12 negative. There were normal values in 34 lepromatous patients 22 of whom were clinically and bacteriologically active and 12 inactive. Normal values were found in 6 out of 9 tuberculoid patients in all of whom the disease was inactive. No definite relationship was found between the serum orosomucoid concentration and the presence or absence of C-reactive protein which was estimated at the same time. *Ernest Muir*

Ramanathan, M. K. Élévation de la cuprémie sérique au cours de la lèpre avec et sans gynécomastie. **[Raised Level of Copper in the Serum in Leprosy with and without Gynaecomastia]** *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 608–10.

The level of copper in the serum varies in a number of diseases and it is suggested that an increase in certain conditions is associated with an excess of circulating oestrogens.

The author, in Pondichéry, India, set out to discover whether an increased level of serum copper occurred in leprosy and especially whether gynaecomastia, often occurring in leprosy, affected this level.

He estimated the amount of copper in the sera of 11 healthy students, 11 patients with lepromatous leprosy but without gynaecomastia, and 13 such patients with gynaecomastia. Those patients having less than 10 gm./100 ml. of haemoglobin were excluded.

The average level of copper in the students was within normal limits, *viz.* 121 μgm./100 ml. In the lepromatous patients without gynaecomastia the mean was 152 μgm./100 ml. and in those with gynaecomastia it was 180 μgm./100 ml. [in the tables, the last two figures have been transposed]. This suggests that chronic leprosy increases the level of serum copper and that if

gynaecomastia is present, it is increased still further, which would seem to indicate an increase of circulating oestrogens which raise the level of serum copper. Statistical analysis indicated that the differences between the 3 groups were highly significant. *H. J. O'D. Burke-Gaffney*

CONVIT, J., LAPENTA, P. & MENDOZA, S. J. **The Methylene Blue Test in Leprosy.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 233–8, 4 figs.

The object of this test is to determine and locate the presence of lepromatous as opposed to tuberculoid or indeterminate structure in leprosy lesions. It consists in injecting intravenously each day a 1% aqueous solution of methylene blue, from 1 to 3 cc. rising to 10 or 20 cc., to a total if necessary of 100 cc. In lepromatous lesions there is blue staining, but no staining in tuberculoid lesions. In borderline cases there is retention of the dye in some lesions or in parts of some lesions. The test is particularly useful in distinguishing reactional tuberculoid cases from borderline when the two resemble each other clinically. It is also useful in detecting residual lepromatous lesions in patients who have partly recovered under treatment. In testing this method the authors injected 65 lepromatous, 37 borderline, 6 indeterminate, and 4 tuberculoid patients. *Ernest Muir*

BASSET, A., CAMAIN, R. & BASSET, Marguerite. **The Initial Forms of Leprosy in Dakar, and their Diagnostic Problems.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 215–23, 9 figs.

At a dermatological clinic in Dakar 5·5% of 1,253 patients seen in its first 10 months were suffering from leprosy, compared with 2·1% suffering from clinical signs of syphilis (although 20 to 30% of the population give positive serological findings). Of the 69 leprosy patients 27 were indeterminate, 31 tuberculoid, 9 lepromatous, and 2 borderline. It is difficult to control leprosy in large towns, as leprosy patients tend to migrate to the towns in hope of alms, and there the lepromatous cases are particularly dangerous as they live in unhygienic surroundings and tend to spread the disease.

The differential diagnosis of each of the 4 forms of leprosy is described in detail, and a further note is given on hyperchromic forms. One particular difficulty in diagnosis is stressed, which arises when corrosives have been applied before the patient comes to the clinic, and also when previously administered cortisone derivatives have completely changed the aspect of the lesions. In early cases biopsy examination should be used before a definite diagnosis is given. *Ernest Muir*

RIDLEY, D. S. **A Bacteriologic Study of Erythema Nodosum Leprosum.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 254–66. [26 refs.]

After a short history of previous work on erythema nodosum leprosum (ENL) the author refers to the "numerical index" in lepromata [this *Bulletin*,

1958, v. 55, 525] and compares it with the bacterial index of ENL biopsy specimens which is calculated by assessing the density of bacilli in different parts of the section and taking an average. The "granularity index" denotes the proportion of solid, fragmented and granular bacilli, and the degree of granulation is calculated from 0 up to 10. In Table 1 the bacterial and granularity indices of ENL lesions and lepromata of 15 patients are recorded along with the duration and type of the ENL lesion. In Table 2 bacterial indices (numerical and granularity) of lepromata, and response to treatment of ENL and non-ENL patients are recorded, cases being divided into lepromatous with ENL, lepromatous without ENL, and borderline-lepromatous.

It is concluded that there were more bacilli in ENL lesions than in "inapparent" infiltrations, but the numbers and granularity of bacilli in ENL lesions were similar to those in non-reacting lepromata biopsied at the same time; that bacilli in lepromata were granular before (not after) the onset of ENL in all cases; that the onset of ENL was preceded by an exceptional fall in the number of bacilli in the skin and this fall in number preceded the granulation of the bacilli; that the occurrence of ENL was closely connected with the actual quantity of non-granular bacilli absorbed from the skin and with the timing of this absorption—a bacteriological relapse may abort the onset of ENL. [This paper is one of particular interest and deserves close study in the original.] *Ernest Muir*

CHAUSSINAND, R., DESTOMBES, P. & BOURCART, N. Transformation en lèpre tuberculoïde de deux cas de lèpre indéterminée préléprómateuse au cours d'un état de réaction. [**Transformation into Tuberculoid of 2 Cases of Prelepromatous Indeterminate Leprosy in the Course of a Condition of Reaction**] *Internat. J. Leprosy*. Wash. 1960, July–Sept., v. 28, No. 3, 224–32, 4 figs.

The authors describe 2 patients with leprosy diagnosed as suffering from the undifferentiated prelepromatous form of the disease. They were bacteriologically strongly positive, and although histological examination showed neither epithelioid nor giant cells, bacilli were present (2 to 3-plus) in histiocytes. In both cases the Mitsuda reaction was negative. In one of these patients the lesions were confined to the lower part of the right leg. During treatment with DDS for 2 years the affected skin became more erythematous, the external popliteal nerve became enlarged and there was steppage gait; bacteriological examination became negative but the Mitsuda reaction was still negative. Later in the course, after a severe reaction with fever and pain the histological examination showed epithelioid and giant cells and the Mitsuda reaction became positive (2-plus). The course of the other case was very similar, except that the reaction was very much more severe and was accompanied by ulceration and necrosis of the affected skin. In this case the bacteriological examination became negative, tuberculoid histology of the lesions appeared, and the Mitsuda reaction became 3-plus with ulceration at the point of inoculation.

The authors suggest that the term "reactional tuberculoid transformation" should be used for this condition as it clearly and simply describes the change taking place, and is a term understood in most languages.

[See also this *Bulletin*, 1959, v. 56, 627.] *Ernest Muir*

BEDDOW, R. M. & TILDEN, I. L. **Malabsorption Syndrome due to Amyloidosis of the Intestine Secondary to Lepromatous Leprosy: Report of a Case.** *Ann. Intern. Med.* 1960, Nov., v. 53, No. 5, 1017–27, 5 figs. [12 refs.]

The authors begin by quoting from other workers' cases of patients who have suffered from a sprue-like syndrome due to amyloidosis of the internal organs, particularly those of the gastro-intestinal tract. They next remark upon the frequency of amyloidosis in leprosy of the lepromatous type, how it had been found among patients with tuberculosis which was a contributory cause of death in 23% of 607 patients dying at the leprosy hospital in Carville; and amyloidosis was present in 17 out of 36 patients at Molokai.

They then describe in detail the history of a patient who suffered from lepromatous leprosy. He was treated for 2 years with Promin which was latterly not well tolerated because of reactions, and later with SU-1906. During the latter treatment he developed anorexia, epigastric pain, occasional nausea and vomiting, and diarrhoea. The drug was therefore discontinued. At that time there was no anaemia, which was against a diagnosis of sprue, but "the presence of albuminuria and moderate microhematuria, associated with a normal blood urea nitrogen and CO_2 combining power, led to a consideration of amyloidosis in the differential diagnosis, particularly in view of the high incidence of this condition in patients with lepromatous leprosy". A biopsy of the bowel confirmed this diagnosis; and when the patient died later an autopsy showed extensive amyloidosis in the heart, blood vessels, abdominal fat, abdominal lymph nodes, spleen, kidneys, and the entire gastro-intestinal tract including the oesophagus and rectum, with lesser amounts in the liver and adrenals. There were massive amyloid deposits in the kidneys. During the administration of SU-1906 there had been rapid enlargement of the thyroid, which was thought to be due to this treatment, but the thyroid was found to be functioning normally. *Ernest Muir*

MEDICAL J. MALAYA. 1960, June, v. 14, No. 4, 249. **Preliminary Report on Diphenyl Thiourea Compound (D.P.T.) Ciba 1906 in the Treatment of Leprosy.**

This brief anonymous note records the treatment with Ciba 1906 (1 gm. daily, increased by 0·5 gm. every 2 weeks to a maintenance dose of 2 gm. daily in two divided doses) of 2 patients with borderline and 10 with lepromatous leprosy. 12 control patients received 800 mgm. DDS by injection weekly in 2 divided doses. Treatment was continued for 1 year; smears were taken every 3 months and biopsy every 6 months.

The 2 patients with borderline leprosy showed remarkable results. Smears became negative and the patients were discharged after one year. The 10 patients with lepromatous leprosy improved considerably both clinically and bacteriologically. The results "were more or less equal to those of Sulphone".

The drug was well tolerated and no skin, liver or kidney damage was noted, other than a mild erythema nodosum in 2 patients on Ciba 1906; but these responded to Stibophen. No drug resistance was encountered.

It is concluded that Ciba 1906 is less toxic than sulphone and at least as effective therapeutically. "The higher cost and inconvenience of daily

administration of Ciba 1906 compared to Sulphones are not considered of much consequence in selective treatment." *H. J. O'D. Burke-Gaffney*

CHAMBON, L. & PESTEL, M. Traitement de seize cas de lèpre lépromateuse par la D-cyclosérine. Résultats après un an et plus de traitement. **[Treatment of 16 Cases of Lepromatous Leprosy with D-cycloserine. Results after a Year or more of Treatment]** *Internat. J. Leprosy*. Wash. 1960, July–Sept., v. 28, No. 3, 239–48, 5 figs.

After treating 16 leprosy patients, of whom 13 were suffering from the lepromatous type, for a year or more with D-cycloserine the authors conclude that there is about a 50% chance that a controllable reaction may cause the rapid disappearance of lepra bacilli from the nasal mucosa and from the skin lesions in a satisfactory and even spectacular manner. When such a reaction does not occur better results may be obtained by combining DDS with the D-cycloserine. But the latter drug is not suitable for mass treatment as reactions have to be carefully controlled. It is suggested, however, that a short hospital treatment with D-cycloserine might be better for very infectious patients rather than a more prolonged out-patient treatment with DDS.

The dose of D-cycloserine was in one group 750 mgm. daily for a week, then 500 mgm., returning to 750 mgm. when the signs of reaction had subsided. In another group a dose of 250 mgm. was given for a week and then 500 mgm. rising to 1 gm. daily. A third series of patients received a combination of D-cycloserine and anti-inflammatory drugs. *Ernest Muir*

PFALTZGRAFF, R. E., with the collaboration of B. U. EKANEM. **Male Hormones in the Management of Leprous Gynecomastia.** *Internat. J. Leprosy*. Wash. 1960, July–Sept., v. 28, No. 3, 249–53. [15 refs.]

19 leprosy patients, who were also suffering from gynaecomastia, were given hormone treatment: 4 with testosterone propionate, 6 with methyltestosterone, 6 with a combination of methyltestosterone and ethinyl oestradiol, and 3 with methandriol. There was a cure in 2 with the first hormone and 1 with the third, but these were early and slight cases. In 5 others there was marked improvement, but it is not certain to what extent this improvement may have been the result of DDS treatment under which the leprosy condition was improving satisfactorily. While hormone treatment may be beneficial for slight or early cases, it is considered that Webster mammaplasty is the treatment of choice in the majority of patients in the present state of our knowledge. *Ernest Muir*

GREBENNIKOV, P. S. **Ways for the Practical Elimination of Leprosy in the Rostov Oblast.** *Internat. J. Leprosy*. Wash. 1960, July–Sept., v. 28, No. 3, 309–13. [Translated from *Sbornik Nauchnykh Rabot po Leprologii i Dermatologii No. 12*. 1959, 81–5.]

After a few preliminary remarks the author finds that concrete ways and means must be found for eliminating leprosy from the Russian Federation. Mention is made of the leprosaria of the North Caucasus and Zagorsk

Leprosy Clinic, with the remark that these "can achieve the practical elimination of leprosy in their areas in 15–20 years". At the Rostov leprosarium the yearly number of new cases had been halved within 10 years and the proportion of lepromatous cases among new patients has been reduced from 72 to 42%. The Rostov leprosarium is now one of the new type—a leprosarium-dispensary, with 127 patients attending the dispensary.

It is proposed to adopt the following measures in the elimination of leprosy: examination of contacts with known patients, a long-term plan of mass examination, control of patients and insurance of regular treatment, separation of active cases, education of patients and the public in endemic areas, control of movements of patients and liaison among the leprosaria, scientific research, courses on leprosy for doctors and the publication of a practical textbook on leprosy for medical workers, vaccination and revaccination with BCG.

[No attempt is made to give any idea of the frequency of leprosy in the Soviet Union.] *Ernest Muir*

NISHIMURA, S., KOSAKA, K. & YASUKAWA, T. **Immunological Relationship between Leprosy and Murine Leprosy. I. Antigenicity of Leprosy Bacillus and Murine Leprosy Bacillus in the Skin Reaction in Guinea Pigs.** *Biken's J.* Osaka. 1960, Aug., v. 3, No. 2, 173–82. [13 refs.]

"Studies were conducted on the immunological relationship between leprosy and murine leprosy. This problem is important in appraising results of experiments using the murine leprosy bacillus.

"Guinea pigs were sensitized with leprosy bacillus, murine leprosy bacillus and BCG, and the Lepromin, Murine Lepromin and Tuberculin reactions examined. Cross immunization was found to occur showing the presence of an immunological interrelationship between these three types. The murine leprosy sensitized and BCG sensitized animals gave the strongest reaction towards the homologous antigen, and lepromin gave values closer to the murine lepromin than to tuberculin."

HELMINTHIASIS

In this section abstracts are arranged as far as possible in the following order:—TREMATODES (*schistosomes, other flukes*); CESTODES (*Diphyllobothrium, Taenia, Echinococcus, other cestodes*); NEMATODES (*hookworms, Ascaris, filarial worms, Dracunculus, etc., Trichuris, Enterobius, Trichinella, etc.*).

DA COSTA, O. R., SILVA, Edith S., BRITO, N., FORTE, O. & LINS, Lizette. Eosinofilia sangüínea: aspectos observados no parasitismo intestinal. [**The Eosinophil Count in Patients with Intestinal Parasites**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1960, June, v. 11, No. 1, 197–205. [17 refs.] English summary.

The intestinal parasites referred to were all helminths and as hookworm is common and often a severe disease in Amazonia the authors attempted to

ascertain what relationship (if any) there was between the eosinophil count and patients infected as follows: Group I, 60 patients infected with hookworm, *Ascaris,* and *Trichuris*; Group II, 28 infected with hookworm and *Ascaris*; Group III, 23 infected with Group I helminths plus *Strongyloides stercoralis,* making 111 patients in all who were in hospitals in Pará state. An eosinophil count of more than 250 per cmm. was taken as positive.

In Group 1, 39 patients were positive for eosinophilia out of 53 tested. In Group II 14 out of 24 examined were positive; in Group III 19 were examined and 16 found to be positive. It was found that in the patients with grave anaemia an improvement in the condition as the result of treatment was accompanied by a rise in the eosinophil count.

The authors conclude that (1) in this region the eosinophil count has a definite relationship to the parasites they considered; (2) the highest incidence was found in Group III infections; (3) improvement in the anaemia was accompanied by a rise in the eosinophil count. This may be helpful in considering the results of treatment. *W. K. Dunscombe*

Da Costa, O. R., Cascaes, O. B. & Silva, Edith S. Estudo comparativo da ação do bephenium hydroxynaphthoate e do iodeto di ditiazanina no parasitismo por helmintos intestinais. [**Comparison of the Action of Bephenium and Dithiazanine in Intestinal Helminthiasis**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1960, June, v. 11, No. 1, 175–86. English summary.

The authors compared the action of bephenium hydroxynaphthoate and dithiazanine iodide on both adults and children suffering from either hookworm alone or combined with other intestinal worms.

For each patient (18 adults and 15 children) ova counts for ankylostome spp., *Ascaris lumbricoides* and *Trichuris trichiura* were carried out by Stoll's method before and 8 days after the end of treatment. The patients were divided into 3 groups according to the number of hookworm ova found and 11 series of 3 patients each were tested; one with bephenium, another with dithiazanine, while the third received no treatment.

Dosage was as follows. Adults received, fasting, 5 gm. bephenium hydroxynaphthoate (=2·5 gm. base) dissolved in water, given for 5 consecutive days; dithiazanine iodide, taken after meals, 300 mgm. on the first day divided into 3 doses, and thereafter 600 mgm. (in 3 doses) for the next 4 days. Children were given bephenium in the same dosage as for adults for 4 consecutive days, the rather bitter taste being disguised by a little sugar. For dithiazanine the dosage varied according to body weight, rising from 200 mgm. for those 15 kgm. or less to 500 mgm. for those 30 kgm. or more for 5 consecutive days, the dose on the first day being about half that of the following days.

Nausea occurred in one adult and in children given bephenium but was not such as to interrupt treatment; with dithiazanine the children surprisingly showed no effects at all, but treatment had to be reduced in 1 adult who had vomiting on the first day and diarrhoea on the fourth day of treatment.

The results showed that bephenium was effective in all 3 types of infection, and that while dithiazanine was more effective than bephenium on *Ascaris* and *Trichuris*, it was not effective for hookworm. *W. K. Dunscombe*

BASNUEVO, J. G. & KOURÍ, A. Acción antihelmíntica del Yoduro de Ditiazanina. [**Anthelmintic Action of Dithiazanine Iodide**] *Rev. Kuba Med. Trop. y Parasit.* 1959, July–Dec., v. 15, Nos. 7/12, 27–36, 4 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"Dithiazanine was administered orally to several parasitics at the following dosage: Adults, 600 mg. daily for 10 days. Children, 10 mg. per pound of body weight daily, for 10 days. The results were as follows:

	Cure Percentage
"Strongyloides stercoralis	94%
Trichuris trichiura	62%
Ascaris lumbricoides	70%
Necator americanus	0
Taenia saginata	0
Hymenolepis nana	0

"Although some of the patients had nausea and vomiting it was not necessary to stop the treatment."

YOKOUCHI, K. [**Study on Parasites in Soil and Dust, and on the Effects of some Vapouring Chemicals on Parasites artificially put in Soil**] *Hirosaki Med. J.* 1960, Nov. 10, v. 12, No. 2, 223–9, 2 figs. [12 refs.] [In Japanese.] English summary *39.

The English summary appended to the paper is as follows:—

"The author searched for parasites and their eggs in soil at 6 places and in dust at 30 places in Hirosaki city and examined the effects of vaporing chemicals on parasites. The results were as follows:

"1. Soil was taken from the surface of the ground and at depths of 10cm, 20cm, 30cm, and 40cm. Eggs of parasites (*Ascaris; Tricocephalus, Trichuris* and *Trichostrongylus orientalis*) were found at 5 places, even at a depth of 40cm.

"2. At 15 of the 30 places, ascaris eggs were found in dust.

"3. Eight vaporing chemicals (vapam, telone, carbon bisulphide, D. D., chlorpicrin, nemagon, fumazone and nemafume 20) diluted to 10 times or 2000 times were sprinkled over the ground and their effects on the parasites (*Ascaris lumbricoides* eggs, *Ancylostoma duodenale* Dubini eggs and larvae, *Rhabditis hominis* and ciliata) buried at a depth of about 20 cm were examined; in addition examination was made in test tubes. Of these chemicals vapam proved the most parasiticidal, telone was next, then bisulphic carbon. D. D. and the others followed. On account of its ready solubility, non-ignitability and slight smell vapam is most suitable."

NELSON, G. S. **Schistosome Infections as Zoonoses in Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, July, v. 54, No. 4, 301–16, 2 figs. [Numerous refs.] Discussion 317–24 [MANSON-BAHR, P.; BOYD, J.; HOARE, C. A.; MANSON-BAHR, P. E. C.; CHESTERMAN, C. C.; WRIGHT, C. A.; LEWIS, D. J.; WOODRUFF, A. W.; MACARTHUR, W. (President); NELSON, G. S. (in reply) with an Addendum by J. R. AUDY].

The recent discovery in Kenya of natural infections of baboons with *Schistosoma mansoni* and of infections of man in South Africa with schistosomes of bovine origin has stimulated the author to review the question of the relationship between man, animals and schistosomes in Africa as a whole. Since this task inevitably involves the use of the term "zoonosis", concerning which in recent years there has been considerable discussion, acrimonious and otherwise, *in litt.* and elsewhere, he finds it desirable to review the meaning of this term and its various connotations, not only in regard to schistosome infections which provide excellent specific examples but also in its wider implications. Having accepted the definition of zoonosis of the WHO/FAO Expert Committee [*Bull. Hyg.*, 1959, v. 34, 1002], in preference to other opinions which ignore the anthropocentric conception of it—an essential ingredient of this particular recipe in the author's view—he proceeds to define the subdivisions of the term as follows:—

(1) the ANTHROPOZOONOSES: infections of man naturally acquired from vertebrate maintenance hosts, *e.g.* rabies and trichinosis;

(2) the ZOOANTHROPONOSES: infections of vertebrates naturally acquired from man, where man is the maintenance host, *e.g.* human tuberculosis in cattle;

(3) the AMPHIXENOSES: infections transmissible between man and vertebrates where maintenance host can be either man or animal, *e.g. Trypanosoma cruzi* or *Schistosoma japonicum*;

(4) the EUZOONOSES: obligatory associations, with man as the definitive host and animal the intermediate host of the same parasite, *e.g. Taenia saginata.*

With the exception of "Amphixenoses" this terminology is not new; the others have been used before but with some inconsistency. The new classification is an attempt to stabilize their meaning so that there may be uniformity of usage and opinion among epidemiologists as to what kind of zoonosis they are dealing with, *e.g.* the direction of the transmission and the functional identity of the maintenance hosts and the incidental hosts. The author discusses the different interpretations of the meaning of zoonoses which have appeared in recent years. Commenting on the classification by KOZAR (1959) [this *Bulletin*, 1960, v. 57, 649] of parasitic zoonoses, *e.g.* "relative zooparasites", "relative anthropoparasites" and "anthropozooparasites", he considers that these terms are unnecessary for this limited group which can be incorporated in existing terms. He proposes the use of the qualification "feral anthropozoonosis" for the transmission from a wild animal to man and "domestic anthropozoonosis" for transmission from a domestic animal.

The main subject of this paper is introduced by a discussion of the validity of 10 species or varieties of schistosomes which have been reported from man in Africa. They fall into three groups, A: those with terminal-spined eggs; B: those with lateral-spined eggs; C: those with eggs having a rudimentary sub-terminal spine. Regarding the 6 species and one variety comprising

Group A, the author believes that further morphological studies will reduce this number. As to Group B, *S. mansoni* is the only representative species with the controversial *S. mansoni* var. *rodentorum* as a doubtful addition; the case for and against the validity of this variety is stated. As to Group C, the reported cases of human infection in Africa with *S. japonicum* and *S. faradjei* (one case only) it is thought that these may have been cases of mistaken identity, in reality due to spurious or real infections with *S. margrebowiei,* a parasite of antelopes with eggs very like those of *S. japonicum.*

The animal hosts of schistosomes reported from man in Africa are distributed among 5 orders of mammals: Perissodactyla, Artiodactyla, Rodentia, Insectivora and Primates, concerning which the author gives a résumé of the literature of these reports and includes his personal observations on the occurrence of schistosomes in Rodentia and Primates. He examined 226 rodents in Kenya, comprising 8 different genera and 10 species and found a schistosome infection in one only, *viz. Dasymys helukus,* from which a single male of the *S. mansoni* type was recovered.

His work on infections of non-human primates relates particularly to *S. mansoni* in baboons which was first reported by MILLER [this *Bulletin,* 1961, v. 58, 221] from Kibwezi in Kenya but he also examined vervet monkeys (39), Sykes monkeys (16) and bush babies (3). Of these animals only 2 were infected (one vervet monkey and one Sykes monkey) and both were infected with terminal spined eggs of the "*S. haematobium* complex". Of the 86 baboons examined, 55% of those from the endemic *S. mansoni* areas were infected. "The majority of infections were light with less than 10 adult worms per animal; but 31 out of 35 infected animals came from areas of low human population density where *S. mansoni* transmission in man is of low endemicity. Four baboons came from Lake Albert in Uganda from an area where *S. mansoni* is much more prevalent in man; all four animals were infected, three heavily; one animal with more than 100 adult worms had extensive damage to the liver. It was obvious that the severity of the pathological changes was proportional to the number of adult worms and the number of ova in the tissues."

Biomphalaria pfeifferi nairobiensis was infected experimentally with baboon *S. mansoni* which was then transmitted to hamsters.

"Present evidence indicates that baboons have contracted their infections from man. They are, however, good hosts of *S. mansoni* and their gregarious nature together with their fondness for living close to snail-infested water might facilitate transmission amongst themselves. In some areas baboons are on the increase. They must be regarded as a potential source of increased *S. mansoni* transmission to man. It is possible that an active zooanthroponosis may be becoming a much more serious amphixenosis."

The methods used for detecting schistosome infections in baboons in the bush, far from laboratory facilities, are described in detail, and the efficiency of the different methods is discussed.

Some of the points made in the discussion were as follows.

Sir Philip MANSON-BAHR: "He [Dr. Nelson] has rightly laid emphasis on the great need for a rigid definition of what is implied by the term 'zoonosis' . . . we are grateful to our speaker that, as far as possible, he has avoided the jaw-breaking expressions so peculiar to this subject".

S. mansoni must have existed purely as a disease of man from very early times and certain monkeys have only recently become infected because of their contact with human beings. "So far, it appears that *S. mansoni* has not been discovered in baboons in areas uninhabited by man."

As to the status of *S. mansoni* in S. America, this is possibly an introduced species still becoming adapted to a new environment or developing into a separate neotropical species.

"Local South American strains of *S. mansoni* develop well in *B. glabratus* from Puerto Rico, but morphologically identical snails from Sao Paulo are refractory. . . . Furthermore, there are physiological varieties of the same snails which affect their capacity as intermediary hosts, and this is a hereditary character.

"The susceptibility of *B. pfeifferi* from Liberia and *B. boissyi* from Egypt to miracidia of South American *S. mansoni* strains would support the idea that some of these schistosomes were originally introduced by slaves from West Africa."

Sir John BOYD queried the statement that canine amoebiasis could be a dog-to-dog infection, for in his experience cysts are not formed in such lesions and therefore dogs must become infected from some non-canine source. He also queried the suggestion that in yellow fever the reservoir of infection may be either man or certain monkeys. "Surely it is neither. The reservoir . . . is the mosquito, which once infected secretes the virus until it dies [for up to 6 weeks, possibly for much longer]. . . . Man and monkey, whose blood is infectious for only 3 or 4 days, do no more than pass the virus from one generation of mosquitoes to another. Does this fact necessitate the creation of another 'nosis'?"

Dr. C. A. HOARE stated that Dr. Nelson's data stressed the interdependence between human and animal infections and that with increasing knowledge, the number of infections supposed to be restricted to man decreases. Although malaria as a disease is confined to man, benign tertian and quartan parasites are also found in chimpanzees and are interchangeable between these hosts; nevertheless malaria is not an anthropozoonosis. ". . . But it is conceivable that man inherited these parasites from his anthropoid ancestors in the course of evolution."

Regarding the diseases peculiar to man ". . . I think there is room in his classification [Dr. Nelson's] for anthroponoses, provided this category is used to denote those human diseases which—though at present restricted to man—have presumably evolved from infections of lower animals (*e.g.* malaria, typhus and relapsing fevers).

"From this point of view, it is also undesirable to exclude diseases of veterinary importance from the concept of zoonoses, thereby perpetuating the artificial separation of human and animal infections in water-tight compartments. Thus, to paraphrase Dr. Nelson's words, I 'unashamedly' associate myself with biologists who regard *Homo sapiens* as 'just another [animal] species'."

Dr. P. E. C. MANSON-BAHR suggested that the baboon is not, in the strict sense, a real parasite reservoir of *S. mansoni* and has only become involved comparatively recently. This is indicated by the nature of the lesions caused by *S. mansoni* in baboons. Further study is required of the severity of the disease in baboons, and comparison with that in man, especially in relation

to the parasite load. The point was made that the isolation from an animal of a parasite which is identical with a parasite of man, does not automatically label that animal as a reservoir host, as the form in the animal may be a different strain which might affect a human host differently. ". . . The only way to settle this point is to study the effects of these strains in man himself."

Dr. C. C. CHESTERMAN: One of the rarer schistosomes of man, *S. intercalatum* Fisher, mentioned by Dr. Nelson in his survey, was diagnosed by finding the eggs in 50% of the children of Yakusu Mission, 15 miles from Stanleyville. "One sheep was infected by feeding it cercariae orally, and it may well be that this endemic area was due to a zoonosis. The many sheep and goats of the village roamed the beaches and small creeks which were used by the children for bathing and as latrines, and the heightened sheep-child contact may have resulted in mutual transferability of the parasite, via the predominant mollusc *P. africana*."

Dr. C. A. WRIGHT expressed concern at part of the statement by Dr. Nelson that "whereas the parasitologist is classifying organisms into groups which are recognizable by constant characteristics the epidemiologist is dealing with rapidly changing situations and a host-parasite complex in one area may be very different in another". The term "constant characteristics" suggested that animal species have got such constant characters, and he disagreed with this. "We are already aware of the enormous range of variation between populations of the molluscan intermediate hosts of schistosomiasis, and I have recently pointed out that there appears to have been a close parallel evolution of the parasites with their snail hosts, resulting in an enormous complex of local races of both the snails and the flukes. . . . The changing situations with which the epidemiologist is confronted are evidence of the differences which exist between populations of the parasites as well as the hosts. Some populations of parasites may be more infective to baboons than others, some populations of baboons may be more susceptible to infection than others."

Dr. D. J. LEWIS: "With regard to the suggestion that the number of species of certain schistosomes should be reduced by introducing trinomial names, is there likely to be enough evidence to decide which forms are subspecies? With reference to the drinking habits of monkeys, many *Cercopithecus aethiops aethiops* visit, and presumably drink from, the Blue Nile".

Professor A. W. WOODRUFF suggested that there might be a parallelism between the marked eosinophilic infiltration in some schistosomal granulomata and not in others and the eosinophilic infiltration in cysticercosis, hydatid disease and other helminth infections; for example, around living cysticerci there is little infiltration but there is much around those that have died. He also referred to Sir John Boyd's account of the control of an outbreak of intestinal amoebic dysentery in dogs by tracing and treating a carrier who prepared their food. "In the light of this experience would Sir John not agree to revise his previously expressed view that treatment of human-food handlers who are carriers of amoebiasis leads to no diminution in incidence of dysentery among those for whom the food is prepared?"

Sir John BOYD, in reply, saw no reasons to revise his opinion. "In the instance I quoted, amoebic dysentery was epizootic in a pack of hounds: the carrier responsible for the outbreak was traced and treated. In man, amoebic dysentery under normal conditions is sporadic, occurring as single widely-separated cases, separated both as regards time and locality . . . and the task of

detecting and eliminating cyst-passers among food handlers . . . is a veritable task of Sisyphus."

The President, Sir William MacArthur, congratulated Dr. Nelson on his laborious and fruitful researches. "But I feel bound to protest against the cumbersome Greek ink-horn words which he has borrowed ready-made from others as headings to his classification, which only obscure what they are supposed to explain.

"We know, of course, that zoological names are not definitions, but it is otherwise with medical terms, or should be . . . they should be precise, intelligible and helpful. But the fabricated Greek words in question have none of these attributes, and to my mind they can only cause confusion; even the meanings which they are claimed to convey can be discovered only by first reading the definition—which is putting the cart before the horse. Beside, the interpretations given are fanciful. Take the first of these as an example—'Anthropozoonosis'. I can understand this only as meaning an inter-transmissible disease of man and animals, that and no more. I had the curiosity to look for this word in some recent medical dictionaries, but found it only in Dorland's where it is defined, 'A disease of either animals or man that may be transmitted from one species to the other'. Which amounts to what I have said already. When the definition quoted in Dr. Nelson's paper is read alongside Dorland's, what is the unhappy student to understand? . . . Without wishing to labour the point further, I must add that I find all these made-up Greek headings puzzling; one of them I can't make sense of at all—perhaps my own fault.

"Today many people seem afraid to use simple English explanatory terms, and prefer the obscurities of a learned language.

"Probably it is the same unwillingness to make use of simple English that has led to the appearance of dreadful formations like 'hospitalize', a word that—if it means anything at all—could only mean 'made into a hospital' . . . The same love of telescoping phrases has given us the lamentable 'arborvirus'. But if 'arthropod-borne' is really too long for this narrow compass of time, then there are other words to be concertina'd in the same way—'mosquito-borne', 'Glossina-borne', 'water-borne', to 'mosbor', 'glosbor', 'watbor'—with all the rest besides. And so, 'On horror's head, horrors accumulate'."

Dr. Nelson (in reply) said: "Sir Philip Manson-Bahr's reference to different strains emphasizes an outstanding problem in our work on the baboon schistosomes. Until we have a less toxic and more effective therapy I do not think we can justify experiments on man".

Commenting on Sir John Boyd's account of amoebiasis in fox hounds: "There seems little doubt that amoebiasis in dogs is generally a 'dead end' zooanthroponosis . . ." but "there is evidence that dogs can become temporary cyst carriers.

"The severity of the pathological changes in the baboons was proportional to the parasite load . . . this must be a reflection of the intensity of transmission balanced by immunity. Dr. Clinton Manson-Bahr suggests that this is probably true in man. . . ."

The speaker welcomed Professor Leiper's comments [which are not reproduced in the text]. "I am afraid that we must admit that very little has been added to our knowledge of the parasites.

" Dr. Hoare's suggestion of ' Anthroponoses ' for purely human infections is logical, but I think it is best avoided ; if this word is used for human infections it is difficult to avoid using zoonoses for purely animal infections."

In reply to Professor Woodruff's query: " . . . although I have not made any detailed study of this subject I have seen plenty of eosinophils around apparently normal ova ; and, on the contrary, many dead ova are often in pseudotubercles free from eosinophils.

" Our president is opposed to the suggested terminology. I admit that it is far from satisfactory, but no simple alternative is available. The terms are not for general use but for specialists studying the epidemiology of particular zoonoses. It is, however, essential that a classification be acceptable in all branches of epidemiology ; by virologists, bacteriologists, protozoologists, helminthologists and also by veterinarians and zoologists who are inevitably involved in the study of zoonoses ".

Professor J. R. AUDY added to the discussion by correspondence, received after the Meeting. He referred to an as yet unpublished paper by MEYER and AUDY on " The Meaning of Zoonosis ", first drafted in 1958. This had two objects: " (a) simply to place on record the historical development of concepts and new terms in this particular field, and (b), while somewhat reluctantly accepting a purely anthropocentric attitude towards the term zoonosis, trying to prevent this anthropocentric usage from obscuring the real theoretical background of the concept of zoonoses ". He stressed the difference between obligatory associations (" euzoonoses ") and the others. Of the latter, there should be a clear recognition in each, of " maintaining-hosts " and " incidental-hosts " ; and since he doubted if people would use the cumbersome terms " anthropozoonoses " and " zooanthroponoses " he suggested that, in general, the general term " zoonoses " should be used while making it quite clear which is the maintaining host and which the incidental host in each association.

He gave examples of the use of simple definitions to replace " anthropozoonosis " etc.: " instead of referring to human tuberculosis in parrots as a ' zooanthroponosis ', it might be both more explicit and less cacophonous to call it ' an avian zoonosis with a human reservoir '.

" Whatever may be decided about usage of terms, it must be understood that the purpose is not to define something happening in nature, but to discover the most useful meaning to be attached to the word ' zoonosis ' and its derivatives. I certainly agree most heartily with Dr. Nelson's insistence on a careful analysis of the situation in each locality, and on sorting out the maintaining-from the incidental-host. Also, his analysis of the situation is both timely and valuable. I am however not happy about such statements as ' A zoonosis must infect man. . .'."

J. J. C. Buckley

BAQIR, H. **Prevalence Survey of Bilharziasis, Ascariasis and Hookworm Infection in Mussayeb Project.** *Bull. Endem. Dis.* Baghdad. 1960, July, v. 3, Nos. 3/4, 24–8.

Mussayeb Project is an irrigation area extending over 750 square km., 80 km. north of Baghdad, to which settlers have been attracted since 1957. Up to

April 1958, out of 826 settlers of all ages whose urines were examined (once only), 32·4% of males and 25·2% of females were infected with *Schistosoma haematobium*. Out of 886 whose stools were examined, 33·1% were infected with *Ascaris lumbricoides* and 19·3% with hookworm. The figures are tabulated for age and sex. *B. B. Waddy*

Capron, A. & Lartigue, J. J. Contribution à la connaissance de la bilharziose vésicale à Madagascar. [**Observations on Vesical Schistosomiasis in Madagascar**] *Arch. Inst. Pasteur de Madagascar*. 1960, v. 28, 157–68. [13 refs.]

In the district of Marovoay epidemiological evidence has pointed to *Bulinus mariei* [a member of the *B. forskali* species complex] as the intermediate host of *Schistosoma haematobium* and this snail has been reported to be infected with furcocercariae. This paper reports the results of an investigation into this problem. Dissections of 2,000 specimens of *B. mariei* were made and the cercariae shed by a further 1,000 individuals were observed. No cercariae of *S. haematobium* were found and the authors are forced to conclude that infection of the snails may be a seasonal occurrence and that positive results might be obtained at other times of year. No other species of *Bulinus* has been found in the area. *C. A. Wright*

Piza, J. de T., Ramos, A. da S., Brandão, C. S. H., De Camargo, Lúcia S. V. & Gonçalves, J. R. Descoberta de um foco autóctone de esquistossomose em Caçapava (Estado de São Paulo—Brasil). [**A Focus of Schistosomiasis in Caçapava, Sao Paulo, Brazil**] *Arquivos de Hig. e Saúde Pública*. S. Paulo. 1960, Sept., v. 25, No. 85, 181–4, 3 figs. English summary.

4 cases of schistosomiasis were found in the town of Caçapava, in the Paraiba Valley, São Paulo: 3 of them were in soldiers of a unit working in the neighbourhood.

Large numbers of snails were found in fields along the banks of the River Paraiba. Of these 5,213 were *Taphius nigricans*, and of 4,671 specimens examined, 15 (0·32%) were found to be infected with *Schistosoma mansoni*. The origin of the infection seems to have been a ditch into which a domestic sewer from a part of the town opened and from which water was used for irrigation of plantations.

The breeding places of the snails were treated with sodium pentachlorophenate and appropriate health education measures were instituted among the soldiers and other members of the population. *H. J. O'D. Burke-Gaffney*

Stirewalt, M. A. & Evans, A. S. **Chromatographic Analysis of Secretions from the Acetabular Glands of Cercariae of** *Schistosoma mansoni*. *Exper. Parasit.* New York. 1960, Sept., v. 10, No. 1, 75–80, 2 figs. [18 refs.]

CLEGG, J. A. **Development of Sperm by** *Schistosoma mansoni* **cultured** *in vitro*. *Bull. Res. Counc. of Israel*. 1959, Oct., v. 8E, Nos. 1/2, 1–6, 2 figs. [10 refs.]

It is now generally agreed that claims for the successful culture of parasitic helminths *in vitro* must be substantiated not only by evidence of survival and increase in size, but also by proof that there has been cellular development (particularly as regards the maturation of the sexual organs) corresponding with the normal pattern of growth of the same species when in a susceptible host. BELL and SMYTH (*Parasitology*, 1958, v. 48, 131) have suggested criteria by which the various stages of cellular development may be judged, and the author of the present paper established these criteria for *Schistosoma mansoni* by infecting a series of white mice with cercariae and then, at short intervals throughout the experiment, noting the condition of those schistosomes which showed the most advanced development. Having established the type and rate of organ development as seen in the normal host, the author then compared these results with those observed when the cercariae were allowed to develop *in vitro*. Since schistosome larvae which have reached the lungs, although seven or more days old, exhibit neither growth nor mitosis, the *in vitro* cultures were started with larvae which had been removed aseptically in large numbers from the lungs of infected mice and then placed in a medium which consisted essentially of inactivated rabbit serum and red cells, together with penicillin and streptomycin added to inhibit bacterial growth. CHEEVER and WELLER [this *Bulletin*, 1959, v. 56, 546], when using a very similar medium, observed a considerable increase in the size of the cultured worms, but sexual maturity was not reached. The author of the present paper at first observed a similar lack of cellular development but when the medium was enriched with amino-acids growth proceeded and 8 testes, without sperm, were produced by the males, while the females developed a uterus but no ovary. Finally, when the medium was changed more frequently, 2 male schistosomes produced sperm in the anterior testes, while the females developed small ovaries. Copulation did not occur. *R. M. Gordon*

GILLET, J., BRUAUX, P. & WOLFS, J. Résultats de prospections malacologiques en profondeur au lac Kivu et recherches sur la survie de *Biomphalaria* en eau profonde. [**Study of the Depths at which Molluscs Occur in Lake Kivu and of the Survival of** *Biomphalaria* **in Deep Water**] *Ann. Soc. Belge de Méd. Trop.* 1960, Aug. 31, v. 40, No. 4, 643–9.

Investigations into the depths at which various species of molluscs occur in Lake Kivu have shown that *Biomphalaria pfeifferi* is normally only found near to the surface: the maximum depth from which a living specimen was recovered was 40 cm. Experiments showed that this same species was able to survive for at least a month at depths down to 15 metres. Maximum depths recorded for other species in Lake Kivu are *Lymnaea natalensis* 0·19 m., *Bulinus coulboisi* 2·70 m., *Gyraulus natalensis* and *Bithynia alberti* 5·0 m. and *Melanoides* sp. 7·0 m. The authors also showed that planorbid snails can be carried to places in the lake where they do not normally occur by attaching themselves to the hulls of small boats. *C. A. Wright*

MORLEY-SMITH, F. & GELFAND, M. **The Establishment of Immunity in Bilharziasis as judged by Age.** *Central African J. of Med.* 1960, Oct., v. 6, No. 10, 447–8, 1 fig.

This a study of the age incidence of schistosomiasis in an endemic focus in Southern Rhodesia. A previous study in the same area revealed a low incidence among infants, suggesting a possible transfer of passive immunity from the mother. If this explanation were correct, it would imply that naturally acquired immunity should tend to give rise to spontaneous cure by middle age. The infections revealed by the survey were 74% at 5 to 9 years, 62% at 10 to 19, 38% at 20 to 29 and "Thereafter the frequency levels itself out between 13 and 20 per cent. and continues at approximately the same level up to 80 years". That some protective or curative powers are built up by the individual is clear, but the existence of the hard core of egg passers at all ages suggests that not every person can overcome his infection. *B. B. Waddy*

SALEM, Emad-El-Din. **The Effect of Adrenalin and Cortisone on Parasitic and Allergic Eosinophilia.** *J. Egyptian Med. Ass.* 1960, v. 43, No. 6, 446–54. [14 refs.]

The fall in circulating eosinophils that occurs in normal subjects after adrenaline or cortisone did not occur in persons with the eosinophilia of asthma or worm infections [mostly schistosomiasis]. This is tentatively explained by supposing that in both disease states the histamine, or related substance produced by the parasite, is a powerful direct stimulus to eosinophil production, over-riding the hormonal control. *Alan B. Raper*

VINKE, B. & JANSEN, W. **Comparison of an Intradermal Test for *Schistosoma mansoni* with the Results of Faecal Examination in Curaçao.** *Trop. & Geograph. Med.* Amsterdam. 1960, Sept., v. 12, No. 3, 217–21.

Curaçao, in which endemic schistosomiasis has not yet been recorded, provides work for large numbers of immigrants, most of whom come from countries where the disease is endemic. Since several potential molluscan vectors of *Schistosoma mansoni* are present in the island it was evident that a simple screening test, such as the intradermal test, would be of great value if reliable in detecting infected immigrants.

140 persons, 40 indigenous patients and 100 immigrants, were subjected to a very thorough examination, which included two intradermal tests, one carried out with the technique of BLAIR and ROSS [this *Bulletin*, 1948, v. 45, 1094] and the other with the technique of PELLEGRINO [*ibid.*, 1959, v. 56, 316 and 547].

In addition the stools of the patients were examined for parasites and "Rectoscopy with three to seven rectal biopsies was carried out in all patients suspected to be suffering from schistosomiasis because of their case history, the bilharzia intradermal test or positive stools, and in some other subjects".

The authors' summary includes the following statement. "When applying the criteria of BLAIR and ROSS we found 15 positive skin tests, when following PELLEGRINO'S method we obtained ten positive results. The latter method did

not yield dubious reactions. The parasite could be demonstrated in only five patients, one of whom had a positive intradermal test according to BLAIR and ROSS and a negative one according to PELLEGRINO. Another patient with a positive test had a heightened alk. phosphatase; although the stools and the rectal biopsy were negative, the patient was strongly suspected of harbouring the disease. The method is a welcome addition as it confirms the results of thorough examination of the stools; because it is an antigen reaction it gives an indication for more detailed examination should the skin test be positive and the stools negative." *R. M. Gordon*

HUTTON, P. W. & HOLLAND, Jean T. **Schistosomiasis of the Spinal Cord. Report of a Case.** *Brit. Med. J.* 1960, Dec. 31, 1931–3, 2 figs. [10 refs.]

After a brief review of the surprisingly few published records of schistosomal involvement of the spinal cord [this *Bulletin*, 1948, v. 45, 1017; 1952, v. 49, 973; 1958, v. 55, 180], the authors report details of such a case seen by them in Uganda. A European aged 73 years, with old injuries of both hips and an ankylosed right knee joint, developed pain, stiffness and cramps in the legs and shortly thereafter overflow incontinence of the bladder and bowel incontinence. The lower limbs became flaccid and palsied with loss of their reflexes. The pressure of the cerebrospinal fluid was normal; initially it contained 90 mgm./100 ml. of protein, 46 mgm./100 ml. of sugar, and 55 lymphocytes per cmm.; 3 weeks later these figures were much lower (10 mgm., 14 mgm., and 15 cells). Neurological investigations suggested a cord lesion about the level of the second lumbar vertebra. X-ray examination of the spine showed an old injury to the body of the second and an old displacement of the fifth lumbar vertebra. A supervening bladder infection, later a cellulitis of the perineum and pressure sores, with progressive deterioration of the general condition, were followed by coma and finally death 10 months after admission.

At autopsy there was no macroscopic evidence of abnormality of the brain or cord. Histological examination revealed granuloma formation with many schistosome eggs, of which one was seen to be terminal-spined, and some degeneration of the tracts in the lumbar and lower thoracic cords. The correct diagnosis, which had not previously been considered, therefore became clear. The possibility of schistosomiasis should be considered in the differential diagnosis of obscure spinal cord lesions in patients who may have been exposed to this infection. *A. R. D. Adams*

NEWSOME, J. & ROBINSON, D. L. H. **Preliminary Observations on Metabolites of Lucanthone.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 582–4.

The authors, using ether extracts of urine from patients taking lucanthone, have separated 11 bands by column chromatography, one of which is lucanthone; most of the others are presumably breakdown products. Accordingly, steps were taken to investigate the metabolism of lucanthone further. When serum from such patients was extracted by the acetone-ether method described by the same authors [this *Bulletin*, 1961, v. 58, 333] the colour was divided

into two fractions which were acid-soluble, and acid-insoluble, respectively. The latter acid-insoluble ether-soluble material also occurred in the serum of 2 normal persons who were not taking lucanthone, and it seemed to be a normal constituent of human serum. In other investigations no evidence could be obtained that lucanthone breaks down in the intestine before it is absorbed.

During tests with flukes of *Schistosoma mansoni in vitro* it was found that 48 hours' exposure to serum from patients, which was estimated to contain 5·6 μgm./ml. lucanthone, caused stupefaction but not death of the worms. On the other hand, worms maintained in guineapig serum and Tyrode's solution to which lucanthone had been added up to 10 μgm./ml. did not paralyse the flukes even in 20 days. This suggests that lucanthone is changed in the body to a form which is more active against the worms. It is suspected that this active metabolite may occur in the acid-soluble fraction extracted from serum.

F. Hawking

Brygoo, E. R. & Capron, A. Aspects expérimentaux du cycle de *Schistosoma mansoni* à Madagascar. [**Experimental Observations on the Developmental Cycle of *Schistosoma mansoni* in Madagascar**] *Arch. Inst. Pasteur de Madagascar*. 1960, v. 28, 169–79. [21 refs.]

Laboratory studies on the Madagascar strain of *Schistosoma mansoni* have shown that the infection matures in mice in 45–60 days, that there is a strong tendency to the development of unisexual infections, that eggs can be recovered from the liver 45 days after infection and from the faeces after 56 days. Most of the mice died in the tenth week of infection. Infections in the snail intermediate host *Biomphalaria madagascariensis* maintained at temperatures between 15 and 20°C. resulted in the production of cercariae after 25 days. It was shown that the temperature at the time of infection of the snails had a great effect on the development of the larval stages of the parasite and the infection rates obtained in experimental infections corresponded closely with natural infection rates found at the *S. mansoni* focus at Ambositra.

C. A. Wright

Weinmann, C. J. **Experimental Infection of Neonatal Mice born of Mothers infected with *Schistosoma mansoni*.** [Research Notes.] *J. Parasitology*. 1960, Dec., v. 46, No. 6, 854.

The author, from the College of Medicine, University of Florida, exposed CFW female mice five or six times at 2- to 3-week intervals to 10 to 12 cercariae of *Schistosoma mansoni* from pools of not less than 8 infected *Australorbis glabratus*. The day after the last exposure infected and non-infected females were mated and litters were born 4 to 7 weeks later. When the offspring were 1 to 6 days old they were infected by placing each mouse in a vial containing 10 to 25 cercariae in a little fresh water; after 30 minutes the young mice were returned to their mothers. The litters were killed 5 to 8 weeks after infection and schistosomes were recovered by perfusion. Litters born of normal females were used as controls.

Three experiments were performed with mice comparable in age and with cercariae from the same pool. Between 15 and 34 mice were used and they

produced 3 to 7 litters. The results are tabulated and show that mean worm burdens for test mice born of infected females and those from normal females were in the three experiments respectively, (1) 1·5 and 1·7, (2) 1·3 and 1·9, (3) 3·5 and 3·5. The differences were not statistically significant. In the three experiments the infected mothers had harboured an average of 4·3, 13·1 and 13·1 worms: the mothers showed numerous lesions.

There were no differences found in worm maturation between the test and control litters. Since MOORE *et al.* (*J. Parasitology*, 1949, v. 35, 434) could not infect mice *in utero* with *S. mansoni*, it seems likely that the parasites recovered from the offspring were from the challenge infection. It was not determined that the infected mothers had acquired immunity, but there is evidence that repeated exposure to small numbers of cercariae does in fact increase the resistance of mice to challenge [this *Bulletin*, 1959, v. 56, 240].

Evidently, under the conditions of these experiments, the young born of infected mothers were as susceptible to *S. mansoni* as those from uninfected mothers. *H. J. O'D. Burke-Gaffney*

HSU, S. Y. Li & HSU, H. F. **Infectivity of the Philippine Strain of** *Schistosoma japonicum* **in** *Oncomelania hupensis*, *O. formosana* **&** *O. nosophora*. *J. Parasitology*. 1960, Dec., v. 46, No. 6, 793–6.

This paper completes our knowledge of the cross-susceptibility between strains of *Schistosoma japonicum* and its snail intermediate hosts; the Chinese, Japanese and Formosan strains have previously been tested by other workers [this *Bulletin*, 1953, v. 50, 226; 1955, v. 52, 381; 1958, v. 55, 1351; 1960, v. 57, 920]. Earlier work has shown that the Philippine strain of the parasite is capable of establishing an infection in 44–75% of *Oncomelania quadrasi*, its normal host. The present paper reports that *O. formosana* is refractory to the Philippine strain but a 20% infection was achieved in *O. hupensis* and 9·6% in *O. nosophora*. The authors tabulate the accumulated results of work on this problem. *C. A. Wright*

HIATT, C. W., HASKINS, W. T. & OLIVIER, L. **The Action of Sunlight on Sodium Pentachlorophenate.** *Amer. J. Trop. Med. & Hyg.* 1960, Sept., v. 9, No. 5, 527–31, 3 figs. [11 refs.]

PITCHFORD (unpublished) has observed that sodium pentachlorophenate was ineffective in killing snails in shallow streams with clear water and he speculated that the compound was destroyed by bright sunshine. The authors accordingly undertook laboratory studies to investigate this possibility.

Aqueous solutions absorb light with a peak at 318 mμ. Chemical tests showed that the substance was broken down by irradiation with light of wavelengths less than 330 mμ. The velocity constant of the reaction was directly proportional to the intensity of the light. The loss of activity in killing snail eggs was proportional to the amount of compound which had been destroyed. It is concluded that in clear shallow water, a considerable amount of the compound could easily be destroyed by direct sunshine; but in turbid water, or at night, little destruction would occur. *F. Hawking*

GILLET, J. Note sur un foyer de bilharziose murine à *Schistosoma rodhaini* Brumpt au Kivu. [**Focus of Murine** *Schistosoma rodhaini* **Infection in the Kivu Area**] *Ann. Soc. Belge de Méd. Trop.* 1960, Aug. 31, v. 40, No. 4, 639–41. [13 refs.]

The English summary appended to the paper is as follows:—

"A very limited focus of *Schistosoma rodhaini* is reported near Bukavu, along the lake Kivu; wild rodents are naturally infected."

LEVINE, D. M. & KAGAN, I. G. **Studies on the Immunology of Schistosomiasis by Vaccination and Passive Transfer.** *J. Parasitology.* 1960, Dec., v. 46, No. 6, 787–92. [21 refs.]

400,000 cercariae of *Schistosoma douthitti* were placed in 5–10 ml. water overnight; they were then removed by centrifuging and the supernatant was used for 3 more batches of cercariae, so that the final fluid contained the metabolic [and disintegration] products of 1·6 million cercariae. In the same way metabolic products were obtained from 300 male and female adult worms. The two fluids were injected with Freund's adjuvant into groups of 15 mice, intraperitoneally once a week for 5 weeks. On the sixth week the mice were exposed to 700 cercariae per mouse, and the results were judged by the survival or death of the mice; deaths of mice dying in less than 8 weeks (0–55% of the group) were ignored as being due to non-relevant causes. The mean week of death of the remaining animals was 10·1 for 10 mice with no incoulations, 10·0 for 4 with sham inoculations, 12·8 for 9 with cercarial antigen, 11·9 for 11 with adult antigen and 12·5 for 8 mice with both antigens. After statistical analysis the authors conclude that the difference between the control and the immunized mice is significant at the 1% level, so that some immunity was produced by the injection of cercarial and worm products.

In another experiment 10 mice were given serum from infected hamsters; 10 mice were given serum from normal hamsters; and 10 mice were untreated controls. Injections were given of 0·25 ml. serum intravenously daily for 4 days before exposure and 0·5 ml. daily for 7 days after exposure. The mice were exposed to 100 cercariae each. The differences of survival of the three groups were insignificant.

It is concluded that mice can be partially immunized by metabolic products from cercariae or adult worms (first experiment) but that it is not possible to show passive transference of immunity (second experiment). *F. Hawking*

KATMINE, D., SAKAGUCHI, Y., INOUE, S. & MOTOMURA, K. [**Studies on Paragonimiasis in Amakusa Island. I. Endemiological Survey on Human Paragonimiasis in Amakusa-Cho**] *Endemic Dis. Bull. Nagasaki Univ.* 1960, Sept. 23, v. 2, No. 3, 212–21, 2 maps. [27 refs.] [In Japanese.] English summary.

Since 1958 a survey of paragonimiasis in man and of metacercariae of *Paragonimus westermani* in the crab, *Eriocheir japonicus*, has been carried out in Amakusa-Cho, Kumamoto Prefecture, Japan.

In 1,919 schoolchildren examined by the intradermal test, 118 (6·1%) were positive, the highest rate (8·42%) being obtained in Takahama district. *Paragonimus* eggs were found in the sputum and stools of 27 out of 82 persons who gave positive intradermal tests.

X-ray examination of the lungs showed pathological changes in more than half of those positive to the intradermal test; in 22 persons the pulmonary changes were typical of paragonimiasis and in most of them eggs were found in the sputum or stool.

19·1% of 1,387 crabs were found to be infected with encysted metacercariae of *P. westermani*, and this incidence rose to 92·1% in crabs caught in 3 rivers in Takahama district where many of the patients were found. There was a striking correlation between the incidence of infection of crabs and of positive intradermal tests in man. The maximum number of metacercariae in a single crab was 440.

Most of the persons with positive findings had a history of having eaten crabs, *E. japonicus*, from the river. The crabs were usually boiled and rarely used to prepare soup: human infection is therefore attributed to contamination of the fingers, table ware and other food in the course of cooking.

It is added that the incidence of positive intradermal tests in boys, which averaged 9·6%, was 2½ times that in girls, probably because boys were more likely to catch crabs and to play with them.

[The abstract has been prepared from the authors' summary in English. Detailed findings are given in 15 tables and 2 maps in the Japanese text.]

H. J. O'D. Burke-Gaffney

GEMMELL, M. A. **Advances in Knowledge on the Distribution and Importance of Hydatid Disease as World Health and Economic Problems during the Decade 1950–1959.** *Helminthological Abstracts.* 1960, Dec., v. 29, Pt. 4, 355–69. [Numerous refs.]

LUBINSKY, G. **A Vegetatively Propagated Strain of Larval** *Echinococcus multilocularis*. *Canadian J. Zool.* 1960, Dec., v. 38, No. 6, 1117–25, 15 figs. (10 on 2 pls.)

AGOSIN, M. & ARAVENA, Luisa. **Studies on the Metabolism of** *Echinococcus granulosus*. **IV. Enzymes of the Pentose Phosphate Pathway.** *Exper. Parasit.* New York. 1960, Sept., v. 10, No. 1, 28–38, 11 figs. [35 refs.]

JANSEN, J., Jr. *Echinococcus granulosus* bij het edelhert (*Cervus elaphus*). [*Echinococcus granulosus* **in Red Deer** (*Cervus elaphus*)] *Tijdschr. v. Diergeneesk.* 1961, Jan. 15, v. 86, No. 2, 82–4.

The English summary appended to the paper is as follows:—

"In the winter of 1959/1960 the author had the opportunity to examine lungs of 53 red deer (*Cervus elaphus*), originating from the Imbosch (Gelderland) for lung-parasites. The occurrence of cysts of *E. granulosus* in two cases

was the most interesting feature. As hydatid disease in man is to be avoided at all costs the author indicates the necessity for meat inspection of all wild animals which are destined for human or animal consumption."

Luccioni, L. A propos d'un cas de kyste hydatique de la tête du pancréas avec ictère. [**Hydatid Cyst of the Head of the Pancreas, with Jaundice. Report of a Case**] *Maroc Méd.* 1960, Oct., v. 39, No. 425, 1074.

Denes de Negri, R. & Luppi, A. Ricerca di eventuali portatori di *Ancylostoma duodenale* e di altri macroparassiti negli operai addetti alle fabbriche di laterizi nella provincia di Rovigo. [**Survey for Carriers of *Ancylostoma duodenale* and Other Intestinal Parasites among Brickworkers in the Rovigo Area, Italy**] *Igiene e San. Pubblica.* Rome. 1960, July–Aug., v. 16, Nos. 7/8, 451–5.

The English summary appended to the paper is as follows:—

"The authors have examined the bowel discharges of 851 workers of 25 lime and brick kilns in the province of Rovigo for detecting the eventual presence of *Ancylostoma duodenale* and the frequency of other intestinal macroparasites. As two cases only of Hookworm presence have been found, one may consider this infestation as practically non-existent in that province. Regarding the other macroparasites the following rates per cent. have been established: *Tricocephalus d.*: 45·7%; *Ascaris l.*: 0·7%; *Strongyloides s.*: 0·7%; *Tricocephalus d.* and *Ascaris l.*: 3·5%; *Tricocephalus d.* and *Strongyloides s.*: 0·35%. One case only of taeniasis. The more frequent parasites (*Tricocephalus d.* alone or associated) do not show any difference among the workers of Upper, Middle or Lower Polesine region."

Farjo, P. D. **The Incidence of Ancylostomiasis in Iraq.** *Bull. Endem. Dis.* Baghdad. 1960, July, v. 3, Nos. 3/4, 29–35. [10 refs.]

Ankylostomiasis is heavily endemic in the south and parts of the central region of Iraq, but uncommon in the northern liwas of Mosul, Erbil, Sulaimaniya and Kirkuk. Although this area contains large rivers and much irrigation, conditions militate against ankylostomiasis. For 7 months of the year the temperature falls below 10°C. for at least part of the time: sometimes it remains low for days. The soil is mostly clay, and dries out thoroughly every year. When rain falls, it does so in torrents which probably wash away many hookworm larvae. Because of the cold climate, the habits of wearing shoes and of using some form of enclosed privy for defaecation are common.

The central and southern areas are warmer and more humid, with mainly sandy soil. Irrigation is more highly developed, and heavy cultivation gives the shade which favours the survival of hookworm larvae. Hygienic conditions in many poor districts are very bad.

Dispensary figures, showing much higher attendances for hookworm in the centre and south, are given, but lack denominators and do not record the actual incidence. *B. B. Waddy*

MONGELLI-SCIANNAMEO, Nicola. Su la patologia del lavoratore agricolo. La sintomatologia neurologica dell'anchilostomiasi: rassegna della letteratura e contributo di un raro caso. [**On the Pathology of the Agricultural Workers. The Neurological Symptomatology of Hookworm Disease: Review of Bibliography and Report of a Rare Case**] *Rass. Med. Indust.* Turin. 1960, May–June, v. 29, No. 3, 205–38, 11 figs. [Numerous refs.] English summary.

After reviewing a good deal of literature on the subject, the author reports a case of his in a peasant aged 50 who had worked since childhood, often in bare feet as is the local custom, on irrigated land which was manured with nightsoil. Like other fellow-workers, he had from time to time suffered from itching in the soles of his feet, and less frequently in the palms of the hands, associated with red vesicular spots. On the 2nd February 1952, this man had to be admitted to hospital with a right hemiparesis, aphasia and some mental confusion. The illness had developed gradually and had set in about a year before with an increasing tiredness and breathlessness, which was at first attributed to obesity and treated accordingly without benefit. There had then developed attacks of unconsciousness of increasing duration which left the patient somewhat confused; on admission, he could neither stand nor sit up.

The blood showed a microcytaemia with $1\frac{1}{2}$ million red cells and a haemoglobin reading of 15%. The leucocytes at 9,600 per cmm. gave a differential count of 73 neutrophils, 16 eosinophils and 11 lymphocytes. The patient was given a number of blood transfusions and treated with iron, liver extracts, B12 and folic acid, but any improvement achieved did not prove lasting.

Hookworm ova and occult blood were found in the faeces, and the administration of carbon tetrachloride brought forth hundreds of *Ancylostoma duodenale*, after which treatment of the anaemia led to recovery.

The author refers to 4 somewhat similar cases reported by others since 1949. Death occurred in 2, a cerebral thrombosis being found post mortem. A search for helminths is called for when anaemia is associated with signs of cerebrospinal involvement. *J. Cauchi*

SCHNEIDER, J. Essai de traitement de la strongyloïdose (anguillulose) par la dithiazanine. [**Trials of Dithiazanine in the Treatment of Strongyloidiasis**] Reprinted from *Thérapie*. 1960, v. 15, 685–91.

18 patients with strongyloidiasis were treated and the author was able to follow up 8. 5 were definitely cured with a total of 3–4·8 gm. of the drug. In 3 it was not successful. Of these one received 18 gm. of dithiazanine in all without any perceptible effect on the embryos; the second and third received 12·6 and 15 gm. in all.

Generally speaking, the drug was well tolerated. Among symptoms of intolerance headache and nausea, and in 3 patients vomiting were noted.

A progressive dosage was adopted— such as a single tablet of 200 mgm. on the first day, and 3 on the 3 following days until the tolerance was established, after which time the treatment could safely be prolonged as long as 20 days. There is no doubt that the advent of dithiazanine marks a definite advance in the treatment of strongyloidiasis. The author thinks that the

physico-chemical state of the intestinal contents, especially the hydrogen ion concentration, should be systematically studied as explaining the somewhat contradictory results obtained with this drug in the treatment of strongyloidiasis. Details are given for each patient.

[See also this *Bulletin*, 1960, v. 57, 819, 827, 925, 1289.]

Philip Manson-Bahr

ASHTON, N. **Larval Granulomatosis of the Retina due to** *Toxocara*. *Brit. J. Ophthalm.* 1960, Mar., v. 44, No. 3, 129–48, 24 figs. (2 coloured on pl.) [32 refs.]

In a histological study of pseudogliomata WILDER (*Trans. Amer. Acad. Ophthal. Otolaryng.*, 1950, v. 55, 99) found nematode larvae in about half the number of patients and in the remainder tissue reactions characteristic of nematode endophthalmitis. These parasites had been mistakenly identified as third-stage *Ancylostoma* larvae. Later in 1952 BEAVER *et al.* (*Pediatrics*, 1952, v. 9, 7) found larval nematodes of the genus *Toxocara* in liver biopsy of 3 patients, after which attention became focused on host-foreign nematodes as agents of human disease.

NICHOLS [this *Bulletin*, 1956, v. 53, 1457] re-examined 5 of the patients with nematode endophthalmitis from Wilder's series and identified the larvae as those of second-stage larvae of *Toxocara canis*, thus showing that this animal nematode, common in dogs, is capable of infecting the human eye.

In the present paper it has been shown that 4 cases of intra-ocular infection by *Toxocara canis* have been demonstrated in England. Case 1, a girl of 8 with visual acuity of 6/60 in the right eye, had an umbilicated tumour at the macula and choroidal disturbance at "6 o'clock". It was thought to be a retinoblastoma and an excision was carried out in October 1952.

Seven years afterwards (in 1959) in 5 out of the 60 stained sections examined, fragments of a nematode larva, resembling that of *Toxocara*, were found. The patient was re-examined for evidence of parasitic infection with negative result. There was no eosinophilia. The family had kept a dog when the child was 8 years old, at the time the eye trouble appeared. The nematode larva was identified by Prof. J. J. C. BUCKLEY (London School of Hygiene and Tropical Medicine) as that of *Toxocara canis* by means of a key provided by Nichols [*ibid.*, *loc. cit.*]. Single lateral alae were visible in the sections and the diameter of 22–22·5μ is the maximum for a second-stage larva of *T. canis*.

Case 2 was a boy aged 16 in the Bristol Eye Hospital. The visual acuity of the right eye was 6/12. In the fundus, just lateral to and slightly below the optic disc was a circular, greyish-white raised area, one disc in diameter, and bearing fine vessels on its surface. Because of the impression that this represented a neoplasm the eye was enucleated in June 1950. The pathological report suggested that it might be a minor form of Coats's disease [retinitis exudativa] or an example of juvenile disciform degeneration.

In 1959, 9 years after enucleation, in 2 sections out of a total of 26 examined, fragments of a nematode larva were found, lying in a small zone of necrotic eosinophilic fibrinoid material. The larva had a diameter of 0·022 mm. and agreed with that of a second-stage *Toxocara canis*. There was no blood eosinophilia and, although the patient had never had a dog of his own, he had been in close contact with that of a neighbour.

Case 3, a boy aged 6, had been treated since 1953 for right convergent strabismus. In December 1958 the visual acuity in the right eye had dropped to 6/60. Ophthalmoscopy revealed a white mass on the temporal side of the right optic disc. On the assumption that it represented a retinoblastoma enucleation was performed in June 1959. The family kept a cat and a bird, but no dog. A blood count showed a slight eosinophilia (7%). 5 out of the 8 serial sections made through the affected area showed a longitudinal section of a fragment of a nematode larva, lying with a clearly defined capsule in the centre of an inflammatory focus, composed of epithelioid and foreign-body giant cells. The measurements of the larva were those of *Toxocara canis*.

Case 4, a boy aged 4, was first seen by the school oculist at the age of 3 for right squint. A grey mass with circular haemorrhage was found at the posterior fundus and was thought to represent a glioma of the optic nerve. The eye was enucleated early in 1956. The fibrous tumour in the macula was seen to connect with a folded detachment of the retina. A small eosinophilic abscess, containing hyaline necrotic material and numerous foreign-body giant cells, was found inferiorly at the periphery of the vitreous. In the 186th and 187th sections the coiled longitudinal sections of a nematode larva were found, but in none of the 320 was there any evidence of another. A blood count showed no eosinophilia and no evidence of parasite infection was obtained on faecal examination. The only pet of the family was a cat. From the measurement of the larva Dr. J. N. OLDHAM reported its resemblance to that of *Toxocara canis*. The oesophageal structure and length agreed with the figures given by SPRENT (*Parasitology*, 1958, v. 48, 184).

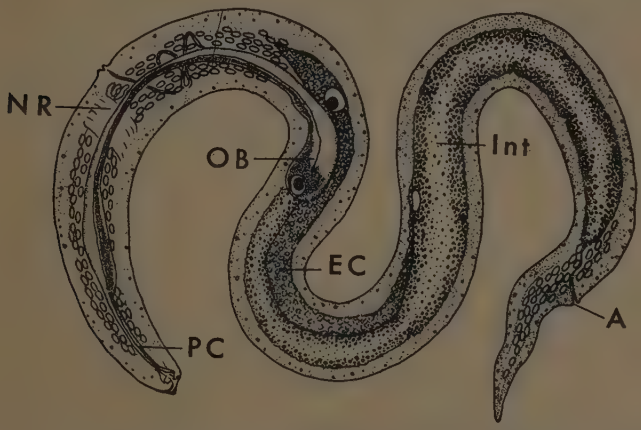
These are examples of ocular involvement in "visceral larva migrans" or "larval granulomatosis" resulting from invasion of human tissues by larvae normally parasitic in lower animals. In this syndrome *Toxocara canis* is believed to be more important than *T. cati*. The former is the commonest cosmopolitan intestinal parasite of dogs, particularly of puppies. The figures of infection are 21% of 1,465 dogs in Indiana, U.S.A. [this *Bulletin*, 1957, v. 54, 848], 20% in Boston [*ibid*., 1956, v. 53, 1151]; 76·5% of 81 puppies in the Philippines (*J. Parasitol*, 1954, v. 40, No. 5, Sect. 2 (Suppl.)); 21·8% of 174 dogs in Melbourne (*Australian Vet. J.*, 1946, v. 22, 85); 82·87% in Calcutta [this *Bulletin*, 1941, v. 38, 374]; 70·8% of dogs in Cambridge (NUTTALL and STRICKLAND, *Parasitology*, 1908, v. 1, 261); 3% of dog faeces in London streets [BROWN and STAMMERS, this *Bulletin*, 1923, v. 20, 455]. In man the parasite is unable to complete its life cycle and rarely, if ever, reaches the egg-laying stage in the human intestine.

Once the ova of *Toxocara* have been swallowed, usually by children of dirt-eating age, they are capable of hatching out in the stomach and intestines, whence the larvae migrate through the intestinal wall into the blood and lymphatics, to become widely disseminated. The prolonged migration is responsible for chronic eosinophilia and there is widespread visceral invasion, particularly of liver and lung. Access to the eye may be gained either *via* the ciliary vessels to the choroid, or *via* the central retinal vessels to the retina and vitreous. The larvae of *T. canis* are active borers.

Histological diagnosis can only be made with certainty when larvae or their fragments have been demonstrated, but this usually entails a prolonged search through hundreds of serial sections; their presence will be suggested by the granulomatous reaction in the eye, together with eosinophilic infiltration or

eosinophilic abscesses, by the presence of foreign-body giant cells and fibrinoid necrosis in immediate vicinity of the larva. Curiously, the right eye was affected in all cases.

Identification of *Toxocara* larvae and their differentiation from those of other nematodes is based on the relative diameters of the body, the presence or absence of lateral alae and posterior excretory columns, and the type of intestine. Diagnosis can generally be made on the basis of one transverse section at mid-gut level, where the significant features are single lateral alae formed by sharp foldings of the cuticle in the lateral line, and an intestine, without lumen, compressed by two large prominent excretory columns which are eosinophilic and non-nucleated. The larva of *T. canis* can be distinguished from *T. cati* only by its slightly greater diameter.



Lateral view of second-stage Larva of *Toxocara canis* (PC, procorpus; NR, nerve ring; OB, oesophageal bulb; EC, excretory column; Int, intestine; A, anus).

It is probable that the larvae are least likely to be found in lesions where the inflammatory reaction is acute, since they may be destroyed by digestive ferments, and are most likely to be discovered when encapsulated, in which state they have been known to survive in the tissues for at least 2 years, this type of tissue reaction serving rather to protect than to destroy them.

Clinical diagnosis is extremely difficult because skin tests and serological tests with specific antigens are unreliable and X-ray examination of no value. The eosinophil count is the most valuable guide and should be carried out in every case of endophthalmitis or suspected case of neoplasm or Coats's disease in childhood, because a definite eosinophilia, together with fever, pulmonary or hepatic involvement, is highly suggestive of visceral larva migrans; yet the degree of eosinophilia, like the severity of clinical symptoms, is proportionate to the severity of the infection.

The incidence of larva migrans in Britain is unknown, but unless it can be shown that *Toxocara* larvae have a predilection for the eye, as they apparently have for mouse brain, it must be commoner than these isolated cases suggest.

This experience underlines the potential danger of household pets to

children. The risk of contact with cats and dogs applies to other parasites, such as *Ancylostoma, Dipylidium caninum* and *Echinococcus granulosus*.

Philip Manson-Bahr

KUIPERS, F. C., VAN THIEL, P. H., RODENBURG, W., WIELINGA, W. J. & ROSKAM, R. T. **Eosinophilic Phlegmon of the Alimentary Canal caused by a Worm.** *Lancet*. 1960, Nov. 26, 1171–3, 1 fig.

An abstract of the authors' earlier paper on human infections with *Eustoma rotundatum*, which is normally a parasite of herrings, appears in this *Bulletin*, 1961, v. 58, 239. The present paper appears to differ from the previous one only as regards the number of infected persons observed: 13 in the present paper, 10 in the earlier one. The signs and symptoms, and the lesions found at operation (for in every instance the condition was sufficiently acute to demand laparotomy) were similar to those already described. *R. M. Gordon*

VAN OYE, E. & PIERQUIN, L. Les filarioses humaines au Congo et au Ruanda-Urundi. Esquisse historique. [**Human Filariasis in the Congo and Ruanda-Urundi. A Historical Sketch**] *Bruxelles-Méd.* 1961, Jan. 8, v. 41, No. 2, 39–53. [61 refs.]

PIRES, F. M., DAVID, J. H. S. & SILVA, J. A. A. O. e. Contribuição para o estudo das filaríases na Lunda. I. Microfilárias sanguícolas: Incidência e espécie infestante na circunscrição do Chitato. [**Study of Filariasis in Lunda, Angola. Incidence and Species of Blood Microfilariae in the Chitato Area**] *Anais Inst. Med. Trop.* Lisbon. 1959, Jan.–Dec., v. 16, Nos. 1/4, 461–79, 3 figs. English summary.

Lunda is a province on the north-eastern border of Angola on the course of the river Casa, adjoining the Congo State.

There a filarial survey was undertaken in the population of the posts of Cachimo, Cambulo, Canzar, Luia and Sombo in the Chitato area. In all, 10,572 persons were examined for microfilariae during the daytime; 5,659 (53·5%) were positive.

It was determined from a microscopic examination of 450 Giemsa-stained blood smears that the species was *Dipetalonema perstans*.

In both sexes the rate of infection increased progressively with age—from zero in children it rose to over 80% in the aged. In children, adolescents and the aged the sexes were equally infected, but during the active period of life the male sex was predominantly infected. On the basis of the census of 1940 the all-round infection rate was estimated at 49·7%. The results are set out in 11 tables and analysed. *Philip Manson-Bahr*

CASTELLANI, A. **Elephantiasis Nostra and Elephantiasis Tropica; a Comparative Study.** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Oct., v. 41, No. 10, 507–22, 2 figs. [19 refs.]

[See also this *Bulletin*, 1961, v. 58, 104.]

NANDA, D. K., ZAFAR, W., SINGH, M. V. & DIWAN CHAND. **Observations on Mass Therapy with Diethylcarbamazine at Barabanki, Uttar Pradesh, under the National Filaria Control Programme.** *Indian J. Malariology.* 1960, June, v. 14, No. 2, 157–63, 1 map.

The filariasis control scheme described in this paper covers an area near Lucknow, India, containing 4 small towns and 360 villages. The parasite is *Wuchereria bancrofti*, and the vector is *Culex fatigans*; the predominant clinical lesion is hydrocele.

Two small areas were chosen for detailed investigation, one near the centre of the controlled zone and a comparison area just outside the control limits. In each of these, representative population samples were examined by night blood surveys before and shortly after the mass treatment; blood films were approximately 20 cmm., and efforts were made to examine the same persons each time. Diethylcarbamazine was administered once daily for 5 days in doses graded according to age, the daily dose for an adult (over 18 years) being 200 mgm.; doses were administered by trained persons making door-to-door visits. The people were warned in advance about possible reactions to the drug, and children below 2 years, pregnant women and sick persons were exempted from treatment. The results are given in the text and shown in a series of tables, and may be summarized thus:—

		No. examined	Mf. rate %	Mean mf. count per positive film (20 cmm.)	*C. fatigans* dissected	*C. fatigans* infected %
Treated area	Before	4,957	10·0	14·3	6,879	1·5
	After	4,608	4·59	6·27	—	—
Untreated area		5,547	10·6	12·1	4,068	0·8
		4,544	8·59	12·22	—	—

From a total population of 307,543, some 4% were exempted from treatment, 14% refused to take the drug, and 24% discontinued taking it, so that only about 58% completed the full 5-day course. Reactions of some sort were noted in about 11% of persons who took the drug.

In discussion, the authors point out the above limitations to the value of mass therapy in a large population, but consider that the transmission of filariasis has probably been reduced. This is a preliminary report, and observations are being continued.

[It is not clear whether the dose of diethylcarbamazine is of a salt or of the base. The reduction of average infection from "14·3 to 6·27 per c.mm. of blood" is stated to be about 69%; this should be "per 20 c.mm." and the reduction is about 56%. It would be interesting to have some indication of the incidence of clinical lesions in a population with the relatively low microfilaria rate of 10%.] *T. Wilson*

KATAMINE, D., YOSHIMURA, O. & SAKAGUCHI, Y. **[Experimental Studies on the Periodicity of Microfilariae. III. Influence of Artificial Hypothermia of the Host upon the Migration of Microfilariae to the Peripheral Blood]** *Endemic Dis. Bull. Nagasaki Univ.* 1960, Sept. 23, v. 2, No. 3, 203–11, 11 figs. [39 refs.] [In Japanese.]

The English summary appended to the paper is as follows: —

"The authors' opinion that the phenomenon of periodicity of microfilariae is attributed to some normal physiological processes of the host had been supported by many experiments previously reported. Furthermore, in this paper, an experiment to observe the influence of body temperature of the host upon the periodicity of microfilariae was added to. Ten dogs infected with *Dirofilaria immitis* were subjected to cooling down using ice-bag and chlorpromazine cocktail.

"Normal temperature of these dogs was approximately 38·5°C. But it fell to 20–30°C. within two or four hours after application of ice-bag, and was so maintained for a 48 hour period. The number of microfilariae per 60cmm of peripheral blood was counted at two hour intervals. It was demonstrated that there was a significant change in the periodicity and number of microfilariae in peripheral circulation. Microfilariae were markedly reduced in the number, going parallel to lowered temperature, and continued to be lacking in periodical fluctuation throughout the whole course of the experiment. On the fifth day after end of the experiment, microfilariae were found to have increased in number, and returned to their normal nocturnal periodicity . . .

"The effect of diethylcarbamazine and acetylcholine in provoking peripheral microfilariae was demonstrated even in such dogs whose temperature was experimentally so lowered."

BERTRAM, D. S. **Some Factors affecting Microfilarial Density and Pathogenicity in Experimental Epidemiology of an Animal Filarioid Infection.** Reprinted from *Proc. Sixth Internat. Congresses on Trop. Med. & Malaria.* 1958, Sept., 5–13, v. 2, 437–43, 2 figs. [14 refs.]

This is a review of the author's work on infection with *Litomosoides carinii* in cotton-rats during the last 10 years. With light infections (12–20 female worms) the number of microfilariae in the blood may be proportional to the number of adult worms, but with heavier infections this is not the case. Reinfection often produces varying degrees of incomplete immunity and the microfilarial density in the blood is correspondingly diminished. In nature the severity of filarial disease is probably affected by the type of transmission, whether seasonal or perennial. According to this conception, incidence of the disease should be greatest with perennial transmission but the microfilariaemia rate and counts might well be low (owing to partial immunity). *F. Hawking*

ROHDE, K. **White Rats infected with *Litomosoides carinii* suitable for Routine Screening of Filaricide Compounds.** [Research Notes.] *J. Parasitology.* 1960, Dec., v. 46, No. 6, 764.

This paper confirms and amplifies results already reported in two previous papers [this *Bulletin,* 1959, v. 56, 961 ; 1960, v. 57, 934]. In later experiments

99 white rats were exposed to mites infected with *Litomosoides*; and 41 contained living worms 91 days later, 38 contained living and dead worms, 1 contained dead worms only and 19 contained no worms. The author considers white rats suitable for chemotherapeutic trials.

[White rats are certainly cheaper and more readily available than cotton-rats which are usually employed, but as stated in the abstract of Rohde's previous paper, most observers, including the reviewer, have found them much less suitable hosts for *Litomosoides* than cotton-rats.] *F. Hawking*

RAGHAVAN, N. G. S., MISRA, B. G. & KRISHNASWAMI, A. K. **Studies on the Effect of Hetrazan on** *Conispiculum guindiensis*. *Indian J. Malariology*. 1960, Sept., v. 14, No. 3, 219–22.

"Studies on the effect of Hetrazan on *Conispiculum guindiensis* are reported.

"Doses, as large as 3 to 10 times that recommended for human infection, produced no effect on either the circulating microfilariae or the adult worms or the embryos in the latter.

"The infection would appear to have restricted use in the routine screening of filaricides."

LAGRAULET, J. & TORROELLA, J. Étude des lésions oculaires onchocerquiennes observées au Mexique (États de Oaxaca et de Chiapas). [**Study of Ocular Lesions of Onchocerciasis observed in the States of Oaxaca and Chiapas, Mexico**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 322–32. [36 refs.]

The authors, having worked in endemic districts in Africa, set out to compare the features of onchocerciasis in Mexico with those of the disease as found in Africa, particularly in regard to lesions of the posterior segment.

In Mexico there are approximately 50,000 *onchocerquiens* in 20,000 of whom the eye is involved. The authors found keratitis frequently, iritis in significant numbers, but in the two districts visited only 13% and 5% of those with affected eyes showed posterior pole lesions.

The character of the chorioretinitis is identical with the African type except that pigment proliferation, as might be expected, is less.

Blindness, despite rumours to the contrary, was rare—less than 1% of onchocerciasis subjects. Why the low incidence of retinal lesions? A break-down of the figures gave 44% of retinal lesions in those aged 40 to 60 years: but conditions of climate and hygiene are such that life is short in these parts and there are few elders. The authors quote the opinion of RODGER (Ghana) [this *Bulletin*, 1958, v. 55, 434] that retinal lesions only seem to occur in conjunction with vitamin A deficiency; and the Mexican view that the lesser gravity of ocular lesions and the low incidence of actual blindness are due to the effective campaign against onchocerciasis. Forward teams (*brigades de lutte*) carry out an active policy of denodulization and diethylcarbamazine treatment; not only among the static inhabitants, but among the migratory land-workers. The authors call this a remarkable organization—a comment which the reader may echo. *A. McKie Reid*

GUPTA, I. M. & RANDHAWA, H. S. **Pathological Changes in the Liver of Wild Rats due to *Capillaria hepatica* with a Note on its Probable Human Occurrence in India.** *Indian J. Med. Res.* 1960, Sept., v. 48, No. 5, 565–70, 9 figs. on 3 pls. [14 refs.]

Capillaria hepatica has been recorded as a parasite of many species of animals (mainly rodents) and also of man. The female worm deposits her eggs in the liver, so that ova do not usually appear in the faeces and perpetuation of the species is normally dependent on the death of the host.

The authors describe, and illustrate, very fully the lesions observed in the livers of rats collected near Delhi and note that these resemble those previously recorded by MCQUOWN [this *Bulletin*, 1954, v. 51, 822] as occurring in the squirrel and in man.

Infection with *C. hepatica* has been recorded in man by various authors [*ibid.*, 1951, v. 48, 183], but in some instances the diagnosis was founded on the finding of the eggs in the stools, and it is probable that some or all of these latter cases were due to the eating of cooked livers of infected rodents. If these doubtful cases are omitted there remain some five records [*ibid.*, 1957, v. 54, 1446], concerning which the authors of the present paper write "The condition in the reported cases was invariably fatal". [So far as the abstracter can discover, one patient, diagnosed by liver biopsy, recovered. It is true that the remaining 4 patients died but the diagnosis in these cases was not made until after death, while the lesions found at the autopsies were such that they might have been the cause of death.]

"Attention is drawn to the fact that the disease is mainly caused in children who may eat dust laden with the eggs of the parasite. The finding is of much greater importance in India as children are known to play in dust laden conditions where the parasite may be found in abundance as in Delhi. Since the diagnosis can only be established by liver biopsy it is suggested that the presence of this parasite should be looked for in all children with symptom complex of hepatomegaly, splenomegaly and hyperglobulinemia particularly in presence of eosinophilia of the blood. It is possible that some of the 'Resistant cases of Pulmonary eosinophilia' may be instances of *Capillaria hepatica* infestation." *R. M. Gordon*

HIRAKAWA, M. [**Experimental Studies on the Third Stage Larvae of *Gnathostoma spinigerum* with special reference to the Pathological Changes of Host**] *Igaku Kenkyu.* Fukuoka. 1959, Mar., v. 29, No. 3, 895–916, 28 figs. [86 refs.] [In Japanese.] English summary.

RIERA ZUBILLAGA, A. Tratamiento de la enterocolitis por tricocéfalos con yoduro de ditiazanina. [**Treatment of Enterocolitis due to *Trichuris* with Dithiazanine Iodide**] *Archivos Venezolanos Puericult. y Pediat.* 1960, Jan.–June, v. 23, Nos. 75/76, 145–50.

The author, in Venezuela, used dithiazanine iodide in the treatment of 10 children (aged 2 to 8 years) suffering from proved *Trichuris* infection with enterocolitis: 7 of them had rectal prolapse. Most of the children suffered

from various degrees of malnutrition, all had a hyperchromic anaemia and 7 had multiple parasitic infections (including *Entamoeba histolytica* in one).

The daily dose of dithiazanine was 100 mgm. per 5 kgm. weight by mouth for 5 days: in one persistent case treatment was prolonged to 10 days. The patient with amoebiasis also received specific treatment.

Diarrhoea disappeared in 2 to 10 days and the rectal prolapse was cured in 5 of the children thus affected. Follow up was possible in 8 patients and 6 of them showed negative stools.

One patient developed urticaria on the fourth day, one suffered from vomiting sufficiently severe to justify suspension of treatment (but the child was cured clinically and parasitologically, despite the incomplete treatment), and the patient who was treated for 10 days developed oedema of the face and lower limbs. *H. J. O'D. Burke-Gaffney*

FERNANDO, P. V. D. **Therapy of Trichuriasis and Ancylostomiasis with Dithiazanine.** *J. Trop. Pediatrics.* London. 1960, Dec., v. 6, No. 3, 80–83. [13 refs.]

The author treated children infected with these worms at the University Unit of the Lady Ridgeway Hospital, Colombo, and at the convalescent home for children.

He emphasizes that *Trichuris* infection can cause bowel disturbances, anaemia, malnutrition, and prolapse.

24 children with this parasite were treated with dithiazanine in a dosage of 5 mgm. per lb. the first day, and 10 mgm. per lb. for 4 more days. The effect was measured by ova counts on the stools by the Stoll dilution technique, before treatment and on the third day after completion of treatment. He regarded reduction in the counts of over 75% as excellent, and 50–75% as good. Of the 24 children 11 were apparently cleared and 3 had more than 75% reduction, 6 had the ova count reduced by 50–75%, while 4 appeared little affected.

He noted a corresponding improvement in the clinical picture.

The usual hookworm species found was *Necator americanus*. Using the same dosage of dithiazanine the author treated 16 cases of hookworm, with even better results: 7 patients showed clearing of stools, 2 over 75% reduction, and 6 good reduction. There was only 1 failure. The author points out that this is at least as good as the results with bephenium [this *Bulletin*, 1959, v. 56, 639]. He concludes that in spite of the need for treatment over several days dithiazanine is the best drug at present for the combination of hookworm and whipworm in children. *A. C. E. Cole*

TRESCA, G. L'infestazione da *E. vermicularis* fra i bambini eritrei. [**Infection with *Enterobius vermicularis* in Eritrean Children**] *Igiene e San. Pubblica.* Rome. 1960, July–Aug., v. 16, Nos. 7/8, 467–70.

The English summary appended to the paper is as follows:—

"The author applies Graham's method to a campaign for detection of infection from *E. vermicularis* among [310] Eritrean children. The conclusion

is that the healthy bearers of Enterobius are, here, not more than in other countries."

KAGAN, G. **A Single-Dose Anthelmintic in General Practice.** [Correspondence.] *Lancet*. 1961, Jan. 14, 112.

The author advocates the use of a single dose of piperazine phosphate and senna (Pripsen) [this *Bulletin*, 1960, v. 57, 742] in the treatment of threadworms. A dosage of 10·4 gm. of the granular preparation containing 4 gm. of piperazine was given to all over 6 years, and 7·8 gm. to the younger children. He points out that, in families, such a treatment given to all is more likely to be effective than the usual 7-day course which is seldom completed by members of the family who were free from symptoms.

If the infection was heavy, or if several children in the family were affected, he gave a second dose after 2 weeks. In 17 cases, diagnosed by symptoms, but confirmed in 13 by the finding of worms, satisfactory cure was obtained by this regimen as judged by absence of symptoms in all the family for 12 weeks. The treatment was also successful in 4 patients with roundworms. No toxic effects were seen. *A. C. E. Cole*

MANCILLA, R. & AGOSIN, M. **The Phosphoglucose Isomerase from** *Trichinella spiralis* **Larvae.** *Exper. Parasit.* New York. 1960, Sept., v. 10, No. 1, 43–50, 6 figs. [30 refs.]

EWERT, A. & OLSON, L. J. **Immunological Tolerance Studies with Mice and** *Trichinella*. *J. Parasitology*. 1960, Dec., v. 46, No. 6, 849–54. [11 refs.]

It is well known that, normally, unrelated animals will reject skin grafts from the same species. However, in 1953 BILLINGHAM *et al.* [*Bull. Hyg.*, 1954, v. 29, 892] showed that skin grafts would take in mice which had been previously injected, during early life, with tissue suspensions of the donor mouse. "In other words, an immunological tolerance had been induced causing the mouse to regard this foreign substance as compatible tissue." Subsequently various workers showed that the technique for inducing immunological tolerance could be extended to include foreign erythrocytes, tumours, chemical allergens, various purified proteins and, although only to a limited extent, to certain microbial agents. However, these observations have not been extended, with the possible exception of the work on trichomoniasis in cattle by KERR and ROBERTSON to protozoa (*J. Hygiene*, 1954, v. 52, 253), while, with the exception of the present work, there is no published account of its experimental application to helminth-vertebrate relationships.

In the present investigation the authors failed to induce acquired immunological tolerance to *Trichinella spiralis* by intracardiac injection of the secretions and excretions of incubated larvae [ES antigen] into newborn mice, which were challenged 6 weeks later by 200 infective *T. spiralis* larvae. Similar negative results were obtained when larval material exposed to sonic radiation was injected.

"The intraperitoneal injections of ES antigen were found to increase significantly the resistance of adult mice to a challenging injection while similar injections of sonicate antigen did not provoke this protection against challenging larvae. The ES antigen appears to have immunogenic properties not found in the sonicate material."

[This very stimulating paper contains much information which is not referred to in the above abstract; it should be read in the original by those interested.]

R. M. Gordon

DEFICIENCY DISEASES

BEGHIN, I. Enquête sur la nutrition et l'état de santé des enfants Warega (Congo belge). [**Survey of Nutrition and Health in Warega Children in the Congo**] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 253–88, 1 graph. [33 refs.]

The Waregas of Maniema in the Congo are a Bantu people whose ways of life and environment are typical of people living in the great tropical rain forests of Central Africa. Their diet is based on plantains, cassava roots and leaves, palm oil, rice, and groundnuts, while children readily take pawpaw, bananas, pineapples and citrus fruits. Eggs are never eaten, and meat and fish only sparingly. Leprosy and onchocerciasis are endemic; malaria is holoendemic. The whole child population (911 children) was studied in a group of villages where there was precise information concerning the number of all children, and of the date of birth of those up to the age of 4 years. The number of absentees at examinations was less than 3%.

As no laboratory facilities were available, the survey was restricted to clinical examinations; these followed a schedule of clinical signs in systematic order. Tables show the frequency distribution of the clinical findings and of haemoglobin concentration (Tallquist) in age-groups. Typical findings were that 9% of the children showed hair signs and hostility, suggestive of mild protein malnutrition; 8% enlarged parotids; 16% dental abnormalities; 23% haemoglobin <70% (Tallquist); 28% splenomegaly; 42% craw craw (*gale*); 8–12% scalp-ringworm and skin mycoses. From these findings, childhood has been divided into 4 periods with characteristic symptomatic differences. From 0 to 6 months—the heaviest incidence of infant mortality, due to acute illnesses, but with a very good state of health and nutrition of the surviving children; from 6 months to 3 years—predominantly poor general health, hair changes, hostility, anaemia, colds, bronchitis and conjunctivitis, umbilical hernia; from 3 years to 9 years—dental abnormalities, enlarged parotids, ariboflavinosis, splenomegaly, ringworm of scalp; 9 years and over—slight reduction of haemoglobin, some parotid enlargement in boys, mycoses of skin, the clinical condition generally approximating to that of the adult.

A significant association between dyschromotrichia and hostility is demonstrated. Provided that a distinction is made between the clearly hostile attitude of a child having the appearance of an angry, miserable, disgruntled, old man, crying with ill temper, and that of a child who is simply frightened

or upset, this hostility appears to be a definite sign of mild protein malnutrition.

Enlargement of the liver occurred but was not related to signs of malnutrition. Avitaminoses and severe kwashiorkor were infrequent. The prevailing syndrome is a mild protein malnutrition as described by SENECAL and AUBRY [this *Bulletin,* 1958, v. 55, 1155] and TROWELL *et al.* [*ibid.,* 1955, v. 52, 496], and it is emphasized that this, rather than severe kwashiorkor, is a fundamental concept for all who wish to understand the pathology of the African child.

T. P. Eddy

RAO, B. R. H., KLONTZ, C. E., BENJAMIN, V., RAO, P. S. S., BEGUM, A. & DUMM, M. E. **Nutritional Status Survey of the Rural Population in Sholavaram.** *J. Indian Med. Ass.* 1960, Sept. 16, v. 35, No. 6, 259–66. [25 refs.]

A health and nutritional survey in Pennathur, previously reported upon [this *Bulletin,* 1960, v. 57, 281] has been followed up by this survey, planned as continuing and confirmatory, in Sholavaram, a village with a population of 2,588 in the same region of South India. A 20% random sample of the whole population was examined.

Details are given of haematological findings and biochemical examinations of serum, and of clinical manifestations of malnutrition. There was a high incidence of conditions traditionally associated with nutritional deficiencies—poor musculature, xerosis conjunctivae with Bitot's spots, xerosis cutis, angular stomatitis, papillary hypertrophy or atrophy, anaemia, caries, and fluorosis. Laboratory examinations showed that blood levels of many subjects were low in vitamin A, serum albumin, iron, haemoglobin, packed cell volume, and mean corpuscular haemoglobin concentration. The authors could not establish a good correlation between clinical and biochemical findings; in particular the skin changes observed did not lead to an accurate assessment of nutritional deficiencies. The findings were generally similar to those at Pennathur.

T. P. Eddy

CHANDRA, H., VENKATACHALAM, P. S., BELAVADI, B., REDDY, V. & GOPALAN, C. **Some Observations on Vitamin A Deficiency in Indian Children.** *Indian J. Child Health.* 1960, Dec., v. 9, No. 12, 589–95.

The recent move of the Nutrition Research Laboratories of the Indian Council of Medical Research from Coonoor to Hyderabad has provided increased opportunities for investigating clinical nutrition problems. The paper under review is concerned with the clinical manifestations of vitamin A deficiency, of which the most important is keratomalacia. The authors point out that vitamin A deficiency in children has received less attention than protein malnutrition, though keratomalacia is a common cause of permanent blindness in South India and hence of considerable economic and social importance. Theoretically at least, it is easier to make good deficiency of vitamin A than deficiency of protein, because sources of pro-vitamin A or carotene are abundant and cheap.

Records of the Paediatric Centre and Institute of Child Health, Niloufer

Hospital, Hyderabad, showed that 551 children with signs of vitamin A deficiency had been treated during the period 1954 to 1958; of these 157 (28%) had keratomalacia, which has been designated by other workers "colliquative necrosis of the cornea". In 79% of cases there was also evidence of protein malnutrition and marasmus was present in 13%. The highest age incidence was in the age-group 3 to 5, with some preponderance of boys probably due to the fact that parents set a higher value on boys than on girls and hence are more ready to seek medical treatment for them. There was no seasonal trend in incidence.

In the Nutrition Clinic of the Nutrition Research Laboratories, Coonoor, vitamin A deficiency, affecting mainly the same age-group, was also seen, but the number of cases and the proportion with keratomalacia were smaller. Intake of vitamin A and carotene is low in both places. A possible explanation of the difference in prevalence and severity is that in Coonoor "mothers started supplementary feeds for their infants by the sixth month, while . . . in Hyderabad, supplementary feeding was not instituted till well after the end of the first year".

Keratomalacia is an acute medical emergency. The best results were obtained when tremendous doses of vitamin A were given—200,000 international units daily for a week by intramuscular injection. Since nearly all children with vitamin A deficiency are in a poor general state of nutrition, treatment should include the provision of a well-balanced diet rich in protein.

W. R. Aykroyd

ABRAMSON, J. H. & GAMPEL, B. **Observations on the Nutritional State of Low-Paid African Labourers in Natal.** *South African Med. J.* 1960, Dec. 10, v. 34, No. 50, 1050–57. [40 refs.]

This long and detailed article deals realistically with the feeding of African labour. The labour groups studied were employed by 6 companies in the neighbourhood of Durban, the great majority of the workers being Zulus, with an average age of 28·6. "They were essentially migrant labourers. Only 6% of the married men and 1% of the unmarried, were living with their families." Cash wages ranged from £1 1s. to £3 13s. per week. Two of the companies provided all the food of the labourers, living in company compounds. Some of the others provided only midday meals, at below cost price, which were in general not popular and taken by only a relatively small proportion of the men. One group, found to have a somewhat better diet than the rest, were not housed by the company, but lived in rented rooms with their families, or in hostels. For 6d. they were supplied with a midday meal, costing about 1s. 6d. to prepare, which 75% took regularly. The predominant food in all the groups was maize, but bread and potatoes were also consumed, in smaller amounts. Foods other than these were rarely eaten. The men employed by 3 of the companies which did not supply a full diet consumed, on the average, meat on 2 days a week, milk on 0 to 0·5, green or yellow vegetables on 0 to 1, and fruit, fish and eggs not at all.

Clinical examinations showed that the men were "obviously a malnourished group". "There was a high prevalence of leanness, of skin and mucosal lesions, and of low total serum-protein concentrations." The authors conclude

that " the high prevalence of signs of malnutrition indicates that most of the men were in a sub-optimal state of health, which might affect their working efficiency ". No cases of pellagra or other flagrant nutritional disease were, however, observed.

Methods of improving the diet are discussed. When managements accept responsibility for feeding the worker, they should obtain competent advice on catering arrangements. Supplementary meals provided below cost price should be palatable and attractive, the workers themselves being consulted about the meals and their preferences taken into account. The authors suggest that there is a strong case for an increase in wages, since present wages do not permit the purchase of a minimum adequate diet. The education of the labourers in better habits of diet is also desirable, and it is recommended that " health educators should be employed by industrial and other employers' organisations, for work in groups of companies ". But while improvements can be introduced by these and other means, this cannot be regarded as a basic solution. The whole system, the authors point out, is at fault, and they quote the following statement from JACKSON [*Bull. Hyg.*, 1954, v. 29, 570]: " the social, medical, economic and moral results of this migratory labour are catastrophic, and the system cannot be condemned too strongly ". *W. R. Aykroyd*

ABRAMSON, J. H., GAMPEL, B., SCOTCH, N. & SLOME, C. **Diet and Serum Protein Levels of Urban Zulu Adults.** *Brit. J. Preventive & Social Med.* 1960, Oct., v. 14, No. 4, 190–95. [24 refs.]

The relationship between diet and serum proteins in 89 Zulu men and 158 women aged 20–64 years, a sample drawn from 1 in 7 homes in a housing scheme with uniform provision of housing, sanitary facilities and availability of health services, was investigated. 50% of the average caloric intake was contributed by maize, with small quantities of green or yellow vegetables, milk, meat and fish. Intestinal helminthiasis, and respiratory infections were common; amoebiasis and schistosomiasis not uncommon; other tropical diseases including malaria were rare. The diet of each subject was assessed by questioning, and classified as " superior " or " inferior " depending upon whether or not 5 pints of milk per week, and meat or fish daily were taken. " Superior " diets so classified were also found to contain more eggs, fruit, green or yellow vegetables, and sugar. The subjects were also classified according to household income, household food expenditure, education, rural or urban childhood environment, proportion of life spent in an urban area, social class, father's social class, and size of household.

There was an association in both sexes between serum-protein levels and diet, serum albumin being significantly higher and globulin significantly lower in men on a " superior diet " than in men on an " inferior diet ". There was a similar association in women, between those who took meat or fish and green or yellow vegetables frequently, and those who did not, but in women only the serum-globulin differences were significant. Of men on an " inferior diet " 74·5% had serum albumin under 3 gm.%, and 31·4% had serum globulin of 4 gm.% or more; for men on a " superior diet " the corresponding figures were 48·6% and 8·1%. When comparisons were made between groups of men on " superior " or " inferior " diets, classified according to the background

environmental and social factors listed above, these relationships of serum protein with diet remained apparent in each instance, with only one exception, the differences between percentages for the two diets being significant in 3 of 17 groups for serum albumin and 8 of 17 groups for serum globulin.

There appeared to be little difference between the two dietary groups in their exposures to infection [no details of clinical histories, or incidence or intensity of current infection are given] and it is concluded that diet is the most important factor in the production of this typical serum-protein pattern among Africans. *T. P. Eddy*

SHAPER, A. G. **Chronic Pancreatic Disease and Protein Malnutrition.** *Lancet.* 1960, June 4, 1223–4, 1 fig.

The author describes chronic pancreatic disease with atrophy, fibrosis and duct calculus formation in 20 adult Africans from the Kampala and Ruanda Urundi regions in East Africa, living on a low protein, low fat, high carbohydrate diet, and not alcoholic.

5 subjects were seen at autopsy, 10 in the diabetic clinic, 2 with malabsorption syndromes and 3 presenting with chronic upper abdominal pain. Most patients complained of abdominal pain, usually only moderate, never the violent pain associated with episodes of acute haemorrhagic pancreatitis.

Radiologically the pancreas displayed changes varying from the fine disseminated calculi in the tail and body to coarse discrete calculi, often very diffuse. Some patients with gross calculi gave no history of abdominal pain.

12 patients had diabetes; 5 had peripheral neuropathies; and one aged 20, bilateral cataracts.

The diabetic picture was similar to that usually seen in the region. Patients were stabilized on 65 units of insulin daily without major control of the diet. 4 presented with ketosis. The serum cholesterol concentration was low. The glucose tolerance test was diabetic in 12.

The pancreas was examined histologically in 7 cases. In the early stages the fibrosis was perilobular and periductal. Late cases showed interacinar fibrosis and obliteration of lobules; the acinar tissue was lost except for occasional residual areas and the islets of Langerhans were scarce, sometimes hypertrophic, hydropic or fibrotic. There was some fatty infiltration but very little cellular reaction. Calcification occurred only in the dilated, cystic ducts.

The author states that over a 7-year period in Mulago Hospital only 4 cases of pancreatic calculi were reported in 3,500 autopsies. 4 patients were diagnosed as having chronic pancreatitis at operation and 2 of these had calculi. In one year all patients attending the diabetic clinic were examined radiologically and calcification was noted in the pancreas in 8%.

The author infers that pancreatitis as such is not the explanation of his cases in which there were no history of alcoholism or signs of biliary tract disease. Severe pancreatic fibrotic changes are seen in kwashiorkor [this *Bulletin*, 1948, v. 45, 633] and similar patterns have been observed in protein malnutrition in African adults [*ibid.*, 1955, v. 52, 496]. ZUIDEMA [*ibid.*, 1959, v. 56, 1050] described equivalent changes with and without calcification in Indonesians and ascribed them to protein malnutrition. The relation between the development of these lesions in the adult and pancreatic damage in

childhood is not established. It appears, however, that pancreatic fibrosis and atrophy are basically the same condition whether or not calcification is present. Calcification is the result, not the cause, of the disorder. *B. G. Maegraith*

HASSAN, M. M. **Kwashiokor in Sudanese Children (Clinical Notes).** *J. Trop. Pediatrics*. London. 1960, Dec., v. 6, No. 3, 98–100, 2 figs.

These notes are not intended to bring out any new features in this condition but to emphasize that kwashiorkor does occur in the children seen at the Paediatric Department in Khartoum, 48 having been diagnosed in 18 months.

The precipitating factors included poor social circumstances, earlier weaning, a poor low-protein weaning diet, and poor maternal diet. The incidence was highest in the trimester October, November, December, following on shortages in the dry months of May, June, July. The majority of patients were $1\frac{1}{2}$–2 years old.

Clinical features included mental changes, first irritability and then apathy, oedema, skin rashes, and hair changes. There were also signs of avitaminosis, ariboflavinosis in 70% and early scurvy in 35%. Liver biopsy showed extensive fatty changes in all cases, while the plasma albumin levels were considerably reduced (0·4 gm. to 3·0 gm., average 1·77 gm. per 100 ml.).

The mortality was 15%, the primary causes of death being intractable gastro-enteritis and bronchopneumonia. *A. C. E. Cole*

VENKATACHALAM, P. S. & GOPALAN, C. **Kwashiorkor in Hyderabad and Coonoor: a Comparison of Salient Features.** *Indian J. Med. Res.* 1960, Sept., v. 48, No. 5, 645–53. [11 refs.]

The authors compare the clinical findings in 107 cases of kwashiorkor investigated in Hyderabad, with 207 cases at Coonoor, 500 miles further south, which were previously reported [VENKATACHALAM *et al.*, this *Bulletin*, 1955, v. 52, 568]; GOPALAN and RAMALINGASWAMI [*ibid.*, 1956, v. 53, 791]. A similar comparison between Coonoor and Uganda was reported earlier [GOPALAN, *ibid.*, 1042].

The patients in Hyderabad were children of poor wage-earning parents. In both Coonoor and Hyderabad, patients were breast-fed until late in the second year, but while in Coonoor supplementary foods were always given by the sixth month, in Hyderabad they were not usually given until well after the end of the first year. A survey of the diet of 58 patients in Hyderabad with that of 30 patients in Coonoor showed that while the intake was 80–260 calories less in Hyderabad, that of other nutrients was the same or higher. An important difference was that while in Coonoor rice was the main cereal, in Hyderabad 30 of the 58 children received jowar (*Sorghum vulgare*) in addition to rice in proportions varying from 3 : 2 to 1 : 1. Though the measured protein intake was a few grammes higher in the Hyderabad patients, the effective amount available on absorption may have been less.

No cases, in either place, occurred in infancy. The peak incidence in Coonoor was between the first and third year and in Hyderabad between the third and fourth year. The ranges, and means related to age of the minimum

body weights reached after the start of treatment are recorded. At all ages Hyderabad weights were lower than Coonoor. Patients at Hyderabad showed a generally higher incidence of deficiency signs than at Coonoor, the comparisons Hyderabad/Coonoor being:—B-complex deficiency, angular stomatitis, cheilosis and glossitis, 34%/15%; skin lesions, 55%/36%; discoloured hair, 32%/13%; hepatomegaly, 23%/10%; rickety deformities of the chest, 18%/0%; mean haemoglobin concentration, 8·3 gm.%/9·3 gm.%; mortality, 15%/9%. Ocular signs of vitamin A deficiency had a similar incidence, 32%/36%, but the predominant form in Hyderabad was keratomalacia often involving both eyes. Though the dietary did not indicate a lower vitamin A intake in Hyderabad, the lateness of supplementary feeding and the low vitamin A intake of pregnant women may affect foetal hepatic storage and the intake of vitamin A in early infancy. Associated with the consumption of jowar, pellagra frequently occurs in Hyderabad adults, and similarly may be related to the higher incidence of skin changes in kwashiorkor. Diarrhoea was a prominent feature (57%/61%) in both series. Steatorrhoea was less common in Hyderabad, but the diarrhoea was more severe, often infective, and sometimes due to amoebic dysentery. Roundworm infection was much less common in Hyderabad patients (18%) than in Coonoor, where it was universal. Plasma proteins and serum albumin were low in all subjects.

Clinical response to treatment with a skim-milk diet of 1,300 calories and 60 gm. protein was as satisfactory in Hyderabad as in Coonoor. *T. P. Eddy*

KARIKS, J. **Kwashiorkor in the Highlands of New Guinea.** *Papua & New Guinea Med. J.* Port Moresby. 1960, Apr., v. 4, No. 1, 5–18, 4 figs. [32 refs.]

Detailed reports describe 7 cases of kwashiorkor seen at the Goroka Native Hospital in the Eastern Highlands District of New Guinea. In the treatment of kwashiorkor in general, the author encountered the usual serious difficulties in the feeding of advanced patients, which were prejudicial to recovery. He therefore started blood transfusions (½ to 1 pint at 20–30 drops per minute) on admission, to treat anaemia, followed in 1–2 days by 100 ml. of concentrated serum albumin. The results were so dramatic and effective that the treatment was adopted as a routine for all cases. With the rapid disappearance of oedema the patients revealed their underlying cachexia, and resembled cases of marasmus. At this stage they became hungry and took food.

Advanced kwashiorkor is seen infrequently in clinical practice as the victims die before they reach hospital. In a field survey of 1,223 children up to 10 years of age, there were 163 (12%) with retarded growth, hypochromotrichia, sparseness of the hair, and anaemia. Of these 163 children with malnutrition 76 (46%) were in the age-group 1–2 years and 153 (94%) were aged 0–3 years; 32 (19·6%) had advanced kwashiorkor, with oedema and skin lesions, and most were aged 1–2 years. Haemoglobin estimations (Sahli) showed that 38·7% of 877 children had a haemoglobin of 10·0 gm. per ml. or less, and serum proteins in hospital patients with kwashiorkor showed the usual low albumin/globulin ratio.

The diet of toddlers in the area is mainly of sweet potatoes with an uncertain amount of breast milk [OOMEN and MALCOLM, this *Bulletin*, 1959, v. 56, 200]

and the disease in New Guinea closely resembles that seen in India, Africa and Jamaica. *T. P. Eddy*

WALT, F. & HATHORN, M. **High Protein Feeding in Kwashiorkor.** *Arch. Dis. in Childhood.* 1960, Oct., v. 35, No. 183, 455–9, 3 figs. [12 refs.]

It has been suggested that a very high protein intake obtained by supplementing skimmed cows milk with concentrated powdered milk-protein, may hasten the cure of kwashiorkor. Patients of Bantu origin admitted to a 6-bed unit at McCord Zulu Hospital, Durban, with kwashiorkor, were allotted alternately to two treatment groups:—SLAM (skimmed lactic acid milk) and SLAM + PS (+ protein supplement "Tervamix" = 68% casein). By the 10th day of treatment, the mean protein intakes were:—SLAM + PS, 3·7 gm./lb. body weight; SLAM, 2·8 gm./lb.; mean caloric intakes:—SLAM + PS, 32·5 cal./lb. body weight; SLAM, 28·4 cal./lb. 30 SLAM and 37 SLAM + PS patients were finally analysed, clinical examination on admission having shown the groups to be similar when compared for age (mean 18–20 months), severity of illness (mild, 30%–32%; moderate, 52%–53%; severe, 16%–17%), need for transfusions, and incidence of infections. All 67 patients recovered and were discharged at the end of the period of observation—28 days.

Comparisons were made of weight change and rise of serum-protein levels. By the 28th day the SLAM + PS group was only 1% above mean admission weight; SLAM was 5·6% above ($P<0·05$). At 42 days there was still a difference but this was not significant. There was no difference between the groups in rate or extent of rise of serum-protein fractions. It is concluded that the protein-supplementation of skimmed milk in the treatment of kwashiorkor is not beneficial.

[PLATT and MILLER (*Proc. Nutrition Soc.*, 1959, v. 18, No. 1, p. vii) have described a method of expressing the protein value of foods in a single figure, which takes account of both quality and quantity of protein in the diet as eaten—the net dietary-protein value or NDpV. The maximum NDpV that can be obtained from any protein, whatever its score, is at 27 protein calories % total calories. SLAM + PS diet from the figures given above for the 10th day gives 45·5 protein calories %; SLAM diet gives 39·4 protein calories %. At a protein score of 80 for milk protein and casein (FAO, this *Bulletin*, 1958, v. 55, 1267) the NDpV for SLAM + PS = 6·5% approximately; NDpV for SLAM = 9 % approximately. On these calculations the nominally higher protein diet is a less efficient provider of protein. Reduction of the proportion of milk protein in either diet to a level of 27 protein calories % by the addition of non-protein calories, would give a NDpV of just over 12%, a more efficient use of protein than appears to occur with either of these diets.] *T. P. Eddy*

SRIKANTIA, S. G. & GOPALAN, C. **Clinical Trials with Vegetable Protein Foods in Kwashiorkor.** *Indian J. Med. Res.* 1960, Sept., v. 48, No. 5, 637–44.

The results of treatment of 83 patients suffering from kwashiorkor with different combinations of vegetable diet at the Nutritional Research Laboratories of the Indian Council of Medical Research are described. Diet 1 contained roasted Bengal gram flour 25 parts, low-fat groundnut 74 parts, lucerne

powder 1 part, with bread and jaggery; diet 2 was similar, low-fat sesame flour replacing one-third of the groundnut flour. The diets contained 1,425–1,430 calories, 70 gm. protein, 11–23 gm. fat, 1,138–1,625 mgm. calcium, and 23 mgm. iron. Diet 3 (groundnut flour only, at 1,380 calories, 70 gm. protein) was given to 11 patients. These results were compared with those of 56 cases previously published (VENKATACHALAM *et al., Indian J. Med. Res.*, 1956, v. 44, 539), treated with Bengal gram and skim milk.

Diets 1 and 2 were nearly as effective in controlling the clinical manifestations of protein malnutrition as were diets with skim milk, and the times for disappearance of oedema, for reaching minimum weight, and for the gain of 1 lb. body weight were not significantly different. Mean serum-albumin levels on the 10th and 30th days of treatment were lower with all vegetable diets than with skim milk. It was surprising to find that the mixed vegetable diets 1 and 2 were inferior in this respect to Bengal gram, and that there was either no rise at all, or an actual fall, in serum-albumin concentration on the 10th day of treatment. With the exception of groundnut flour only (diet 3), the differences between all diets were much smaller by the 30th day of treatment. The continuation of diet 2 at a level of 70 gm. protein per day for 45 days, showed a significant increase in serum-albumin concentrations between the 30th and 45th days, producing serum-albumin levels comparable to those of the children treated with Bengal gram. Increase in the protein in diet 2 to an intake of 100 gm. per day produced a significantly higher serum-albumin concentration on the 30th day, but no such difference on the 10th day of treatment. Diet 3 (groundnut flour only) showed much poorer results at all stages of treatment.

Theoretically, it should be possible to overcome the limitations of vegetable proteins by judicious combinations of vegetable foods to give a balanced composition of essential amino-acids. The addition of groundnut flour to Bengal gram, with or without sesame flour, in these experiments did not contribute to, indeed actually appeared to retard, serum-albumin regeneration in the initial stages, and groundnut protein appears to be inferior to skim milk and Bengal gram. It is possible that the rate of serum-albumin regeneration on certain diets is relatively slower than the speed with which plasma volume is returned to normal, and this might have caused the drop in serum-protein concentrations on the 10th day in several patients on diets 1 and 2. The results obtained from increasing protein to 100 gm. per day were at variance with those reported with skim milk [JAYALAKSHMI *et al.*, this *Bulletin*, 1957, v. 54, 1455] in which a similar quantitative increase in protein did not produce a greater rise in serum albumin. This would appear to be due to the different biological values of the proteins. *T. P. Eddy*

MACDONALD, I. **Comparison of Changes in Serum Proteins during Early Treatment in Kwashiorkor and Marasmus.** *Arch. Dis. in Childhood.* 1960, Oct., v. 35, No. 183, 448–54, 4 figs.

The dietary defect leading to marasmus is quantitative, a deficiency of calories as well as of protein; the defect leading to kwashiorkor is qualitative, an imbalance caused by protein deficiency with a relative excess of carbohydrates. The clinical picture in these two types of malnutrition is strikingly

different. This study of serum proteins during early treatment of the two diseases (made in the paediatric department, Hôpital A. le Dantec, Dakar, French West Africa) was designed to show whether there were any differences in protein metabolism in the two diseases that might be concerned in the aetiology of the differing clinical signs.

A kwashiorkor group of 7 patients, all with skin and hair changes, gross oedema, and apathy, were compared with a group of marasmic patients who had none of these signs and who were mentally alert on admission. Daily blood samples were taken, from before the start of treatment, on a standard high-protein diet, until the 14th day in hospital, Total serum proteins were estimated by refractometry followed by paper electrophoresis. Comparisons are made with mean values obtained from 41 normal African children (DAVIN, *Contribution a l'étude électrophorètique du serum sanguin chez l'enfant africain normal et dans les états de malnutrition* (*Kwashiorkor*). Thesis 1955. University of Bordeaux).

Tables are given to show mean daily values of serum proteins in both diseases for the 14 days of treatment. The mean values (gm. %) may be summarized as follows:—

	Kwashiorkor		Marasmus		Normal
	1st day	14th day	1st day	14th day	
Total protein	4·26	5·93	5·45	6·39	7·37
Albumin	1·23	1·91	1·99	2·38	3·28
Alpha-1 globulin	0·46	0·64	0·60	0·51	0·57
Alpha-2 globulin	0·59	0·94	0·68	0·86	0·97
Beta globulin	0·56	0·90	0·63	0·85	0·92
Gamma globulin	1·42	1·54	1·55	1·79	1·62

Before treatment, the percentage rise or fall from normal values of different protein fractions in kwashiorkor/marasmus was: albumin $-62\%/-39\%$; α_2 and β $-39\%/-32\%$; α_1 $-19\%/+5\%$; γ $-12\%/-4\%$ In the two conditions, α_2 and β seem to be linked and equally affected; the reduction in albumin is much more marked in kwashiorkor; the least proportional changes were seen in α_1 and γ globulins. During treatment the total proteins increased at a fairly constant rate, except for a slight reduction in the first 2 days of treatment (perhaps due to increase of blood volume), but the rate of increase of all serum proteins is greater in kwashiorkor than in marasmus, except for the γ globulins whose rate of change is the same.

The pattern of the serum proteins in both conditions is the same, except that the reduction in serum albumin is greater in kwashiorkor. This suggests that protein metabolism in both differs only in degree, though kwashiorkor may be a more acute form of malnutrition than marasmus. The apparent links in the extent of the change from normal between α_1 and γ globulin, and between α_2 and β globulins, with their similar rates of response to treatment, suggests that the metabolic processes concerned in the production and utilization of these two pairs are closely allied. It is possible that γ globulin is only influenced by the infection contracted by the child, and not by the inadequate protein intake. The clinical differences between marasmus and kwashiorkor may be due to some factor other than protein metabolism, possibly the relative excess of carbohydrate. *T. P. Eddy*

KEELEY, K. J. **Prognosis of 'Nutritional' Heart Disease in the Bantu. Report of a Case of Chronic Reversible Heart Failure.** *South African Med. J.* 1960, Dec. 17, v. 34, No. 51, 1072–4, 4 figs.

OHFU, K. [**A Clinical Study of Beriberi (Slight Form) in Children**] *Igaku Kenkyu.* Fukuoka. 1959, Mar., v. 29, No. 3, 1042–60, 4 figs. [35 refs.] [In Japanese.] English summary.

SPRUE

MILANES, F. Cambios en la epidemiología y comportamiento clínico del sprue ocurridos en Cuba, durante las tres décadas 1927–1957. [**Changes in the Epidemiology and Clinical Features of Sprue in Cuba between 1927 and 1957**] *Archivos Hospitales Universitarios.* 1960, May–June, v. 12, No. 3, 125–44. [23 refs.] English summary.

Tropical sprue has been reported in Cuba since the beginning of the present century. Then it was a severe disease with an incidence of 4 to 5% of the hospital population. The incidence has decreased progressively during the decades (1927–37, 1937–47 and 1947–57) from 3% to 1·17%, and 0·36% of the hospital population. Males have predominated and the age incidence varied from 41 to 70 years. Most patients observed in the first decade were white descendants from the Canary Islands; there was an absence of Negroes: later the number of mulattoes and Negroes increased. The mortality has been much reduced and during the last 15 years has been non-existent.

There is no evidence that the disease has ever been contagious.

During this last decade typical cases have rarely been seen.

The statement is made that an absolute cure does not exist, and relapses are always possible.

The epidemiology and clinical features are discussed and compared for each of the 3 decades separately. *Philip Manson-Bahr*

RAJAN, K. T., RAO, P. S. S., PONNUSAMY, I. & BAKER, S. J. **The Oral Glucose-Tolerance Test in Tropical Malabsorption Syndrome.** *Brit. Med. J.* 1961, Jan. 7, 29–31, 1 chart. [25 refs.]

50 patients with the tropical malabsorption syndrome, defined by steatorrhoea with a total daily fat excretion of more than 5 gm. on a diet of 50 gm. fat, were compared as to their oral glucose tolerance with 24 apparently normal subjects as controls.

The glucose was estimated on venous blood drawn before 50 gm. glucose was taken in 200 ml. water but after 10 hours' fasting, and also at 4 half-hour intervals after taking the glucose.

The mean maximum rise in the steatorrhoea group was 22·6 mgm./100 ml. compared with 44·6 mgm./100 ml. in the controls. The authors suggest that the dividing line between a "flat" curve and a normal curve should be fixed at a rise of 25 mgm./100 ml. or less. 66% of the patients with steatorrhoea failed to reach this level and only 16% of the controls.

The scatter in the results both in the cases of steatorrhoea and the controls prevents the test giving a clear cut diagnosis in the individual subject, though the difference in the means of the groups is said to be highly significant. [A scatter diagram is given but not the actual figures.]

Also of interest was the difference in the fasting blood sugars. In the steatorrhoea patients the mean was 72·4 mgm./100 ml. while in the controls the mean was 93·8 mgm./100 ml. The authors suggest that a fasting blood sugar of 80 mgm./100 ml. or less is suggestive of malabsorption, this low level occurring in 76% of the steatorrhoea patients and in only 8% of the controls.

They also discuss the possible explanations, and point out that the accepted radiological signs are not always correlated with the degree of malabsorption.

A. C. E. Cole

Doig, A. & Girdwood, R. H. **The Absorption of Folic Acid and Labelled Cyanocobalamin in Intestinal Malabsorption. With Observations on the Faecal Excretion of Fat and Nitrogen and the Absorption of Glucose and Xylose.** *Quart. J. Med.* (n.s.) 1960, July, v. 29, No. 115, 333–74, 3 figs. [Numerous refs.]

The absorption of folic acid and labelled cyanocobalamin was studied in 65 patients with intestinal malabsorption (26 cases of idiopathic steatorrhoea, one tropical sprue, 3 persistent coeliac disease, 20 cases of malabsorption following surgical interference and 15 cases of anatomical intestinal lesions) and in 50 controls (25 with Addisonian pernicious anaemia). Examinations were also made of faecal excretion of fat and nitrogen and of absorption of glucose and xylose.

The authors refer to the first three groups of cases as examples of malabsorptions of the "sprue" type. In these, folic acid absorption was impaired in 25, and absorption of cyanocobalamin in 12, and in the majority there was malabsorption of xylose and glucose, usually associated with folic acid malabsorption. The disturbance of absorption of the sugars was not always in parallel.

None of the surgical cases showed folic acid malabsorption and only 3 of the cases with anatomical lesions. Absorption of cyanocobalamin was impaired in 14 surgical cases, 9 of which had developed megaloblastic anaemia. (One patient with idiopathic steatorrhoea had Addisonian pernicious anaemia.) Improvement in absorption occurred in the presence of intrinsic factor. In half these patients the faecal excretion of fat was increased. Malabsorption of cyanocobalamin was present in 13 of the 15 anatomical cases.

Bacteria from stagnant areas of small intestine could remove the vitamin from culture media and under suitable conditions could synthesize folic acid. The authors consider that the main sites of absorption of folic acid and cyanocobalamin respectively are the jejunum and the ileum.

The combined results of absorption tests with folic acid and tagged cyanocobalamin are useful diagnostically as shown in the table.

Result of absorption test	*Interpretation*	*Examples*
1. Malabsorption of cyanocobalamin corrected by:		
(a) intrinsic factor	Failure of secretion of intrinsic factor from gastritis, mucosal atrophy or surgical resection	Pernicious anaemia Idiopathic steatorrhoea Gastrectomy
(b) antibiotics or surgery	Bacterial uptake of cyanocobalamin in stagnant loops of small intestine or short-circuit of ileum	Strictures or fistulae of ileum; jejunal diverticulosis, ileo- or jejuno-colostomy
2. Malabsorption of cyanocobalamin which cannot be corrected as above	Loss of ileum by resection or disease	Surgical resection of lower ileum Idiopathic steatorrhoea Tropical sprue
3. Malabsorption of folic acid	Extensive lesion of upper intestinal mucosa, leading to absorptive failure	Idiopathic steatorrhoea Coeliac disease Tropical sprue

B. G. Maegraith

HAEMATOLOGY

BARUA, R. N. & FOLL, C. V. **Anaemias of Pregnancy in Upper Assam and Upper Burma.** *J. Trop. Med. & Hyg.* 1960, Oct., v. 63, No. 10, 225–32, 1 fig. [29 refs.]

Data were collected of 449 Asian women at antenatal clinics for the wives of oil company employees in Digboi, Upper Assam, and the degree of anaemia was compared with that found in a similar survey of 263 women in Upper Burma [this *Bulletin,* 1959, v. 56, 581]. The average Hb level (8·8 gm./100 ml.) in the former group was 2·0 gm. lower than in the latter. Unfortunately, although many clinical facts are recorded, the material is not treated statistically; and also, as is so common in comparisons of this sort, there were many variable factors. The diet in Assam was poorer, conditions of stress were greater, hookworm was commoner (19·2% as against nil), roundworms were more frequent; but sweating was less, and amoebiasis much less. Malaria was virtually absent in both localities. Thus different combinations of "tropical" conditions can, in the absence of malaria, produce severe anaemia in pregnancy. The authors make the important remark that the more severely anaemic group was that in which child-bearing began younger, leaving no time for the restoration of the iron stores after the demands of growth had been met. *Alan B. Raper*

TONDO, C. V. & SALZANO, F. M. **Hemoglobin Types of the Caingang Indians of Brazil.** *Science.* 1960, Dec. 23, v. 132, 1893–4. [17 refs.]

"We studied the hemoglobin types of 440 individuals (306 unrelated) cytologically and by paper electrophoresis. These included 334 (252 unrelated) putative 'full bloods'. No abnormal types were found."

JACKSON, F. S., LEHMANN, H. & SHARIH, A. **Thalassaemia in a Tibetan discovered during a Haemoglobin Survey among the Sherpas.** [Correspondence.] *Nature*. 1960, Dec. 24, v. 188, 1121–2, 1 fig.

For cases in Gurkhas, see this *Bulletin*, 1960, v. 57, 938. Gurkhas are racially distinct from Sherpas.

NEEB, H., BEIBOER, J. L., JONXIS, J. H. P., SIJPESTEIJN, J. A. K. & MULLER, C. J. Thalassemie met lepore hemoglobine bij twee Papoea-kinderen in Nederlands Nieuw-Guinea. [**Thalassaemia with Lepore Haemoglobin in Two Papuan Children**] *Nederl. Tijdschr. v. Geneesk*. 1961, Jan. 7, v. 105, No. 1, 8–14, 7 figs.

The English summary appended to the paper is as follows:—

"In a Papuan family two children have the clinical symptoms of Cooley's anaemia. Their blood lacks normal adult haemoglobin; besides foetal haemoglobin, it also contains an abnormal haemoglobin, which has been identified as Lepore haemoglobin. A concentration of c. 20 per cent. Lepore haemoglobin was demonstrated in the blood of the parents and of a number of relatives. This familial anomaly is discussed in connection with current views on Cooley's anaemia."

ALLISON, A. C. **Observations on the Sickling Phenomenon and on the Distribution of Different Haemoglobin Types in Erythrocyte Populations.** *Clin. Sci.* 1956, v. 15, No. 4, 497–510, 5 figs. [32 refs.]

Advantage was taken of the fact that 0·3% NaCl will lyse all oxygenated red cells, including those of sickling subjects, but not cells sickled by anoxia. By suitable arrangements, therefore [the paper should be read in full], it is possible to separate the cells less susceptible to sickling from those more susceptible, in various types of sickle-cell disease. When this was done, it was always found that the less susceptible cells showed slightly more Hb F and slightly less Hb S than did the original mixture of cells of both types. This unexpected result indicated that the distribution of haemoglobins was not constant from cell to cell. But the author also notes that the technique did to some extent effect a separation of cells on the basis of their age, the younger cells being less readily sickled; [and, it may be added, less easily lysed]. *Alan B. Raper*

OBER, W. B., BRUNO, M. S., WEINBERG, S. B., JONES, F. M., Jr. & WEINER, L. **Fatal Intravascular Sickling in a Patient with Sickle-Cell Trait.** *New England J. of Med.* 1960, Nov. 10, v. 263, No. 19, 947–9, 3 figs. [11 refs.]

"A fatal case of mesenteric occlusion associated with widespread intravascular sickling in a fifteen-year-old Negro is presented. Hemoglobin electrophoresis revealed the underlying hemoglobinopathy to be sickle-cell trait with an A + S pattern.

"From this case as well as others previously reported it appears necessary to scrutinize cases of sickle-cell trait more closely and perhaps to modify previous opinions of the benign nature of this inherited state.

"It is suggested that samples of blood be taken at autopsy for hemoglobin electrophoresis in cases of Negro patients dying suddenly or from causes not immediately apparent."

See also p. 526, BECQUET *et al.* [**The Correlation between Tropical Ulcer and Sickling in the Cameroons**].

MCCORMICK, W. F. & HUMPHREYS, Eleanor W. **High Fetal-Hemoglobin C Disease: a New Syndrome.** *Blood.* 1960, Dec., v. 16, No. 6, 1736–44, 3 figs. [23 refs.]

"A case of interaction of the genes for hemoglobin C and 'high fetal' has been reported, with an incomplete family study. The 'high F' gene seems to behave as a dominant one.

"A discussion of the relationship, if any, with this disease to 'classical' C-thalassemia was presented. The evidence is inconclusive, but this case does not fit the picture of C-thalassemia as previously reported and is considered to be a separate condition."

WASI, P., GITHENS, J. & HATHAWAY, W. **Hemoglobin J in an American Caucasian Family of Swedish Ancestry.** *Blood.* 1960, Dec., v. 16, No. 6, 1795–9, 2 figs. [25 refs.]

The haemoglobin of a healthy Swedish-German male aged 30 was found to consist of Hb A and J [this *Bulletin,* 1960, v. 57, 633]. The identity of the latter was confirmed by comparison with a known specimen; it formed 52% of the total pigment. The father of the propositus proved to have Hb A and J, the mother and sister Hb A only. All were normal haematologically.

Alan B. Raper

VENOMS AND ANTIVENENES

ZARAFONETIS, C. J. D. & KALAS, J. P. **Serotonin, Catechol Amines, and Amine Oxidase Activity in the Venoms of Certain Reptiles.** *Amer. J. Med. Sci.* 1960, Dec., v. 240, No. 6, 764–8, 1 fig. [13 refs.]

DÉTRAIT, J., IZARD, Y. & BOQUET, P. Relations antigéniques entre un facteur léthal du venin d'*Echis carinata* et les neurotoxines des venins de *Naja naja* et de *Naja nigricollis.* [**Antigenic Relationship between a Lethal Factor in the Venom of *Echis carinatus* and the Neurotoxins of the Venoms of *Naja naja* and *N. nigricollis***] *C.R. Soc. Biol.* 1960, v. 154, No. 6, 1163–5.

CHRISTENSEN, P. A. **The Scope of South African Anti-Snakebite Sera.** *South African Med. J.* 1960, Aug. 13, v. 34, No. 33, 684.

The following antivenenes are produced in South Africa:—

(1) polyvalent, prepared from the venoms of *Hemachatus haemachatus* (ringhals), *Naja nivea* (Cape cobra) and *Bitis arietans* (puff adder);

(2) polyvalent, prepared from the venom of all the above, plus that of *Bitis gabonica* (Gaboon adder);

(3) monovalent, prepared from the venom of *Echis carinatus*;

(4) monovalent, prepared from the venom of *Dendroaspis jamesoni* (mamba).

The polyvalent sera are active against the venoms of the snakes mentioned and also *Naja nigricollis* (the spitting cobra), *Naja haje* (the Egyptian cobra) and *Naja melanoleuca* (the black-lipped forest cobra). They are also capable of neutralizing the venoms of Indian cobras. The second polyvalent serum is more effective against the venom of the Gaboon and rhinoceros vipers (*Bitis nasicornis*). Both act moderately against the venom of *Causus* spp. (the night adder).

Neutralization of *E. carinatus* venom requires the specific monovalent serum, which is partly effective against the venom of *Cerastes* spp.

The monovalent serum prepared from *D. jamesoni* is useful in bites from this reptile but not from other mambas, including *D. angusticeps*. Polyvalent serum has little effect but should be used if the monovalent serum is unobtainable. Large scale production of other monovalent mamba sera is hampered by the difficulty in obtaining adequate supplies of venom.

Minimum potency requirements for antivenenes have been introduced in the Union. It is to be hoped that other countries will follow this lead.

[See also this *Bulletin*, 1955, v. 52, 421.] *B. G. Maegraith*

BALOZET, L. La mesure de l'efficacité thérapeutique des sérums antivenimeux. [**Measurement of Therapeutic Efficiency of Antivenenes**] *Arch. Inst. Pasteur d'Algérie*. 1959, Sept., v. 37, No. 3, 387–400, 4 figs. [22 refs.]

Bivalent antivenom is produced by contemporaneous injection of the venoms of *Cerastes cerastes* and *Vipera lebetina*. The author examined the efficiency of the serum with each venom separately in groups of male mice weighing about 18 gm. each. The LD50 for each venom was ascertained and groups of animals were injected intracutaneously with this dose of venom only. In other groups given the same dose, 0·5 ml. serum was given (intracutaneously but in a different place) at the same time and at 15 min., 30 min., 60 min., and 120 min. later. In each case the LD50 was calculated.

The serum was less effective for the lebetine venom than for that of *C. cerastes*. The equivalent neutralizing values *in vitro* were very different from the therapeutic activity. The therapeutic action in a given case could be measured best by calculating the index of efficacy, *i.e.* LD50 of toxin + serum divided by the LD50 of the toxin alone. This would be useful for comparing batches of serum, but would not be directly applicable to man.

B. G. Maegraith

GUPTA, P. S., BHARGAVA, S. P. & SHARMA, M. L. **A Review of 200 Cases of Snake Bite with special reference to the Corticosteroid Therapy.** *J. Indian Med. Ass.* 1960, Nov. 1, v. 35, No. 9, 387–90.

Approximately 25,000 deaths from snake bite occur each year in India [PORGES, this *Bulletin*, 1953, v. 50, 847]. Cobra, krait and vipers, principally Russell's viper and *Echis*, are the most common and responsible for practically all the snake bite deaths in the country.

Snake venom is complex and its toxic action is due to proteolytic enzymes, phosphatidases and neurotoxins and the results depend upon the quantity and quality injected, producing symptoms within 10 minutes to 2 hours after the bite.

The patients studied ranged between 3 and 80 years in age. The incidence was 21 in the 1–15 age-group, 118 in the 16–30, 39 in the 31–45, 19 in the 46–60 group and 3 in those over 60 years. 164 were males and 36 females.

The seasonal incidence increased in June and reached its peak in August.

In 32% of the patients bites were inflicted on fingers and toes, in 48% on hands and feet and in 20% on the remaining parts of the body. The exact type of snake causing the bite could not be ascertained (except in 3 instances) and could only be guessed at from symptoms and signs.

The neurological manifestations consisted of muscular weakness, blurred speech, inability to swallow, dribbling of saliva, shallow breathing followed by respiratory failure and sometimes death. Bleeding from the bite wound occurred in 24 patients, gross haematuria in 8. There were 35 cases of macroscopic or microscopic haematuria and the coagulation time varied between 14 and 50 minutes. In 3 patients the bleeding time was increased, varying between 6 and 9 minutes. One of these also had a purpuric rash.

Ligation or application of tourniquet was used as a first-aid method in 60% while incision, suction and lavage with potassium permanganate was a universal measure. Antitetanic serum was injected in 95%; intravenously, 10–110 cc., in 91%. 12 patients were found to be sensitive to this serum; in 3 desensitization was resorted to and 7 others developed urticaria. For infected lesions penicillin was used in 57%. In addition, some patients with severe local oedema, fever, haemorrhage or neurological manifestations were given 50–100 mgm. cortisone, intramuscularly every 8 hours, or 5–10 mgm. prednisolone every 6 to 8 hours.

11 of the 200 patients (5·5%) died, 9 within 6 hours of admission. 189 (94·5%) recovered without sequelae. Among those treated with corticosteroids there were no deaths and the control of bleeding was earlier, reduction of oedema and pain quicker, and there were no allergic reactions.

Philip Manson-Bahr

BENYAJATI, C., KEOPLUNG, M. & SRIBHIBHADH, R. **Viper Bite in Thailand: with Notes on Treatment.** *J. Trop. Med. & Hyg.* 1960, Nov., v. 63, No. 11, 257–60, 1 fig. [13 refs.]

In Thailand most of the 200–300 fatalities due to snake bite which are reported annually are attributed to 3 species of vipers, the green pit viper, *Trimeresurus gramineus*, Russell's viper and *Ankistrodon rhodostoma*, the last

2 being highly venomous. Since 1956 treatment with antivenene has been replaced by the use of cortisone combined with antivenene, or by cortisone alone.

The immediate symptoms of envenomation by these species comprise intense local pain which spreads rapidly up the limb, local oedema which quickly increases, ecchymoses and bleeding from the fang punctures. Tissue necrosis, thrombophlebitis, intravascular haemolysis and a general bleeding tendency appear on the second to third day. Severely affected patients may bleed from the alimentary or urinary tract within 24 hours, and in them shock is usually severe. No neurological symptoms were observed in the series of patients here reviewed.

It is the practice of the authors to apply a tourniquet to the bitten limb as soon as possible, after which cortisone is administered alone or together with 30 ml. of polyvalent or antineurotoxic serum. The results of steroid therapy impressed the authors, for it seemed to arrest the bleeding within 3 days and to inhibit tissue necrosis. The platelet count returned to normal in 4–10 days. Threatened gangrene was often averted, and a further valuable action was the prevention of serum sickness. Under this therapy only 1 patient, suffering severely from Russell's viper bite, showed sustained renal damage. Transfusion of fresh blood was reserved for the treatment of grave haemorrhagic states, while an anticoagulant, Hirudoid, was used in severe thrombophlebitis.

[It is a pity that this paper does not include the data on which these statements are based.] *J. H. Walters*

MULLINS, J. F. & NAYLOR, D. **Successful Management of Cobra Bite with Cryotherapy.** *J. Amer. Med. Ass.* 1960, Nov. 26, v. 174, No. 13, 1677–9.

The authors point out the rarity of cobra bite in the U.S.A. since the Elapidae are not indigenous to that country. In addition to the very dangerous neurotoxin, the venom contains many other factors including a cardiotoxin, a haemolysin, an anticoagulant, an inhibitor of respiratory enzymes, and a range of enzymes. These may exert significant effects.

The case of a 17-year-old youth is reported, who was bitten on the index finger of the left hand while handling a 3-foot-long cobra at a fair. He immediately applied a strangulating tourniquet to the finger proximal to the fang punctures, and was admitted to an emergency medical centre 10 minutes later. There cryotherapy was immediately begun by placing the boy's hand in ice and water; the tourniquet was released after 5 minutes but then replaced for a further 15 minutes. 100 units of corticotrophin gel were injected. intramuscularly and the patient was admitted to hospital.

Cryotherapy was maintained for 34 hours by immersion in iced water of the hand and later the forearm also. Additional treatment comprised an infusion of 100 mgm. hydrocortisone in 500 ml. of 5% dextrose, 1,500 units of tetanus antitoxin and a daily dose of 600,000 units of penicillin. 9 hours after envenomation cobra antivenene (Pasteur Institute, Paris) was injected, 10 ml. being injected intravenously and 10 ml. intramuscularly. This was repeated 24 hours later. A transfusion of 500 ml. of blood was also given.

During the next 24 hours a total of 2,000 ml. of 5% dextrose was administered by continuous infusion, together with 400 mgm. of hydrocortisone, after which steroid therapy was continued with triamcinolone 20 mgm. 4 times daily by mouth.

No evidence of neurotoxic effects was observed during the first 24 hours, and none subsequently developed. Local swelling developed up to the shoulder on removal of the limb from the bath of iced water after 24 hours, so 12 hours later cooling was reinstituted by placing the limb in a plastic sleeve packed with crushed ice. This treatment was maintained for a further 64 hours.

Gangrene of the distal part of the finger which had been rendered avascular developed and necessitated amputation at the proximal interphalangeal joint. There was evidence of slight haemolysis, with a rise in serum bilirubin from 0·6 to 0·85 mgm. per 100 ml., while a reticulocytosis of 3·4% developed. The prothrombin time fell to 60% of normal.

After amputation, recovery was complete. The authors discuss the advantages and disadvantages of cryotherapy [see also this *Bulletin,* 1957, v. 54, 1119].

[Cryotherapy may well have limited local oedema but it is not possible to attribute to it alone the absence of general systemic and neurotoxic symptoms. The prompt application of the strangling tourniquet, immobilization, antivenene and steroid therapy must have contributed to the favourable result.]

J. H. Walters

KINGSTON, C. W. & SOUTHCOTT, R. V. **Skin Histopathology in Fatal Jellyfish Stinging.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, July, v. 54, No. 4, 373–84, 12 figs. (10 on 3 pls.) [34 refs.]

Specimens of skin including wheals and other superficial lesions, were examined in 2 fatal cases of jellyfish stinging in Queensland coastal waters. One victim, a female child aged 11, died within a few minutes of being stung. The other, a male aged 38, died in less than 45 minutes. Autopsy showed pulmonary oedema and shock in both cases. Very adherent jellyfish tentacles were found hanging to the legs which were covered with linear reddish-brown streaks and wheals.

Sections of the epithelium showed oedematous stratum corneum and thinned degenerate Malpighian layers, with shrunken cells, blurred intercellular bridges and pyknotic nuclei. Subepithelial tissue was unaffected. On the surface of the affected areas of skin were numbers of oval objects, faintly eosinophilic, which were identified as nematocysts, some still undischarged, others intermediate or completely discharged with the threads penetrating at angles into the skin beneath. Threads penetrated into the epithelium or well into the dermis (up to 200 μ). In some places they were continuous with the oval or circular structures on the surface.

The nematocysts were identified as microbasic mastigophores with large distinct elongated capsules. They matched the nematocysts on the tentacles of the Cubomedusae (sea-wasps), *Chironex fleckeri* and *Chiropsalmus quadrigatus*. These are discussed fully and illustrated.

The authors consider that the skin reaction was not anaphylactic, but purely

toxic. Some very powerful poison was obviously injected by the nematocysts. Fatal issue may be determined by the dose of toxin injected.

The features are illustrated in 10 clear photomicrographs.

B. G. Maegraith

HUTTON, R. F. **Marine Dermatosis. Notes on "Seabather's Eruption" with *Creseis acicula* Rang (Mollusca: Pteropoda) as the Cause of a Particular Type of Sea Sting along the West Coast of Florida.** *Arch. Dermat.* 1960, Dec., v. 82, No. 6, 951–6, 4 figs. [18 refs.]

TOXOPLASMOSIS

INTERNATIONAL CONGRESS OF PAEDIATRICS, VIII. Copenhagen, 1956. **Human Toxoplasmosis. Proceedings of the Conference on Clinical Aspects and Diagnostic Problems of Toxoplasmosis in Paediatrics.** Revised and edited 1959 [SIIM, J. Chr. (M.D.)]. 220 pp., illustrated. 1960, Copenhagen: Munksgaard, Denmark.

This conference was held in Copenhagen in July 1956, but in order to meet requests for publication of its proceedings the papers are now presented under one cover, revised and brought up to date.

The aim of the meeting was to bring together specialists on toxoplasmosis to make known the clear-cut facts concerning the present knowledge of the disease. The conference was attended by 19 representatives from 12 countries, all of them well-known experts with whose work readers of this *Bulletin* will be familiar.

After a brief statement of the present status and problems of toxoplasmosis in paediatrics, the work is divided into 6 parts. The first part deals in 6 papers with congenital toxoplasmosis. The second (6 papers) discusses the clinical and diagnostic aspects of acquired toxoplasmosis, with special emphasis on lymphadenopathy. The third part consists of a single paper on treatment and the fourth of 2 papers concerned with ocular toxoplasmosis. Epidemiological aspects are discussed in 3 papers in the fifth part, and finally there is a sixth part containing 4 papers on laboratory diagnosis and a short discussion.

All these papers deal both with the experiences of the authors themselves and with the literature, and a valuable feature is the considerable collection of references to published papers given by the various participants.

Such a wide coverage of a subject not yet fully recognized in many countries will be a most useful source of reference to those who require authoritative information on all aspects of human toxoplasmosis.

H. J. O'D. Burke-Gaffney

VARELA, G., ROCH, E. & VAZQUEZ, A. Virulencia, cultivo, polisacaridos, toxinas y la prueba del colorante estudiado, con una cepa de *Toxoplasma gondii*. [**Virulence, Cultivation, Polysaccharides, Toxins and the Dye Test studied in a Strain of** *Toxoplasma gondii*] *Salud Pública México*. 1960, Jan.–Mar., v. 2, No. 1, 135–9. [22 refs.]

The authors describe observations and experiments on a strain of *Toxoplasma* isolated in Mexico, whose virulence became stabilized after 258 passages through rats, which died regularly 4–5 days after inoculation. This strain was virulent to hamsters, rabbits and guineapigs but not infective to reptiles. It was successfully grown in cultures of human embryonic tissues. By staining with "Alcian Blue 8GN 150", the presence of a polysaccharide was demonstrated in the toxoplasms, while no experimental evidence could be obtained of the presence of "toxotoxin".

The same strain was also used in a serological survey of persons from various parts of Mexico and of rats from Mexico City by the dye test. Positive reactions were obtained in 37·5% of 104 children and in 26·7–64·7% of 740 adults, and in 15·9–34·6% of 360 wild rats. However, since many of the rats were infected with other parasites (sarcosporidia, *Trichinella*, filariae or intestinal flagellates), the true significance of these serological reactions could not be determined. *C. A. Hoare*

WERNER, H. Zur Frage der Übertragung von *Toxoplasma gondii* auf dem Geschlechtsweg. [**Transmission of** *Toxoplasma gondii* **by the Genital Route**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1960, v. 11, No. 1, 12–21, 11 figs. [11 refs.]

It has been previously demonstrated that in female rodents suffering from toxoplasmosis all parts of the genital organs are invaded by the parasites. In order to ascertain whether *Toxoplasma* can be transmitted directly from male to female during the sexual act, the author inoculated male mice and hamsters intraperitoneally, intravenously and intratesticularly with strain "BK" of the parasite isolated from the peritoneal exudate of infected mice. The animals were killed 96–110 hours later and their genital organs were fixed and sectioned, and examined microscopically for the presence of toxoplasms.

The parasites were found chiefly in the parenchymatous and connective tissues, *viz.* in tunica albuginea, septula testis, and in the intermediate layer of the testes, as well as in the epididymis, the sheath of vas deferens and accessory glands, in all of which reproduction was taking place. Pseudocysts occurred chiefly in the intermediate layer of the testes, near the basal membrane surrounding the tubuli contorti. It is suggested that toxoplasms emerging from the infected tissues into the lumen of the ductus deferens are carried away and discharged with the semen during ejaculation. *C. A. Hoare*

KULASIRI, C. **The Nature of the Cytoplasm-Modifying Antibodies.** *Parasitology*. 1960, Nov., v. 50, Nos. 3/4, 419–23, 2 figs.

Sera from rabbits which had been immunized with a strain of *Toxoplasma* were fractionated by alcohol precipitation. The fractions which contained the

gamma globulins were found to have the highest titre when tested by the dye test of SABIN and FELDMAN; it was therefore suggested that the cytoplasm-modifying antibody involved in this test was associated with the gamma globulin in the serum.

[See also this *Bulletin*, 1957, v. 54, 1237; 1958, v. 55, 816, 1275.]

W. E. Ormerod

KABELITZ, H. J. Die diagnostische Bedeutung und klinische Beurteilung der *Toxoplasma*-Seroreaktionen und des Toxoplasmin-Hauttests. [**Diagnostic Significance and Clinical Implications of the Serological Test and Skin Test for Toxoplasmosis**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1960, v. 11, No. 3, 287–98. [Numerous refs.]

FRENKEL, J. K., WEBER, R. W. & LUNDE, M. N. **Acute Toxoplasmosis. Effective Treatment with Pyrimethamine, Sulfadiazine, Leucovorin Calcium, and Yeast.** *J. Amer. Med. Ass.* 1960, July 30, v. 173, No. 13, 1471–6, 2 figs. [18 refs.]

Although sulphadiazine and pyrimethamine have been shown in mice to be successful in the treatment of acute toxoplasmosis [this *Bulletin*, 1956, v. 53, 367] their effect in this condition in man had, it is stated, not been proved. An accidental laboratory infection of a young adult woman, however, provided an opportunity for demonstrating its value.

Antibodies as measured by the dye and haemagglutination tests appeared 9 and 14 days respectively after inoculation. The toxoplasmin skin test was negative after 20 days and positive 4 months after inoculation.

Treatment with standard doses of pyrimethamine and sulphadiazine was begun on the 9th day after infection and was rapidly followed by defervescence of fever. On the 18th day of treatment with 25 mgm. of pyrimethamine and 4 gm. sulphadiazine daily the white blood cell count was 3,750 per cmm. and the platelet count 94,000 per cmm. having initially been 5,700 and 115,000 respectively. After treatment with yeast and daily doses of 5–15 mgm. leucovorin calcium these counts became normal.

Clinical and laboratory details of the acute illness following accidental infection are given. The latter was caused by inoculation of a culture into the fifth finger of the left hand and was followed 5 days later by fever and axillary and cervical lymphadenopathy. The patient's dose had probably been between 1 and 100 mouse LD50. *Toxoplasma* were isolated in mice from the patient's venous blood obtained 9 and 10 days respectively after inoculation, *i.e.* just before treatment was started and 15 hours thereafter.

The patient became pregnant 18 months later and the infant died on the 4th day after birth. Autopsy revealed an enlarged cor biloculare with single quadricuspid atrioventricular valve and coarctation of the aorta, proximal to a patent ductus arteriosus. No evidence of toxoplasmal infection was found at autopsy or by mouse inoculation. In view of previously reported large series of patients who had had toxoplasmosis and who had subsequently given birth to normal infants [*ibid.*, 1953, v. 50, 567], it is thought that there was no causal relationship between the toxoplasmosis and the congenital malformation in this case.

A. W. Woodruff

DOMINGUEZ CARMONA, M. Quelques données sur la toxoplasmose expérimentale chez la souris. I. Localisation dans la moelle osseuse. II. Localisation élective au niveau du poumon des souris inoculées par voie veineuse. **[Some Data on Experimental Toxoplasmosis in Mice. I. Localization in Bone Marrow. II. Selective Localization in the Lung of Mice inoculated Intravenously]** *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 32–5.

When inoculated intraperitoneally into mice, an Oubangui strain of *Toxoplasma* was very rarely detected by direct examination of the bone narrow of infected mice, but the presence of parasites could be demonstrated in 5 out of 10 cases by subinoculation of such bone marrow material.

After intravenous inoculation of mice with peritoneal exudate of infected mice (and, in 2 cases, with teased-up bone marrow and brain respectively), parasites were found in the lungs of 45·4% of the mice, and in the peritoneal cavity of 16·6%. Intraperitoneal inoculation of organ suspensions from these mice into other mice produced infection in most of the latter (as shown by further subinoculation), but microscopical examination revealed parasites only in the lungs. This organ is therefore the site of predilection for toxoplasms, which can be detected in the lungs more readily than elsewhere. *C. A. Hoare*

DERMATOLOGY AND FUNGUS DISEASES

RILEY, O., Jr. & MANN, S. H. **Brain Abscess caused by *Cladosporium trichoides*. Review of 3 Cases and Report of Fourth Case.** *Amer. J. Clin. Path.* 1960, June, v. 33, No. 6, 525–31, 4 figs.

Cladosporiosis of the central nervous system, which is due to *Cladosporium trichoides* Emmons, has been recorded only occasionally [but this is the 8th and not the 4th case]. In all these cases some part of the brain or its meninges has been the site of lesions.

The patient was a white man aged 24 years, a farmer from Crowley, Louisiana. He became ill on September 7, 1957. X-ray examination of the cranium revealed a space-occupying lesion in the right frontal lobe of the brain. Accordingly, a craniotomy was carried out, and when an encapsulated mass was discovered in the anterior part of the right frontal lobe it was removed. The patient subsequently made a rapid recovery.

The specimen removed was an ovoid fragment of tissue, 3·0 by 2·0 by 2·0 cm. The central portion contained an abscess cavity in which necrotic tissue was present and large numbers of branching, septate hyphae, 2–4 μ in diameter. Many giant cells which were also present contained large numbers of hyphae. Culture produced "dark brown, felt-like [fungal] colonies, 1 to 2 mm. in diameter" at 8 days. The fungus grew well on all the culture media. Branching conidiophores bore oval conidia, 4 to 10 μ by 2 to 6 μ at 10 days. The macroscopic and microscopic features agreed with those described for

Cladosporium trichoides. Inoculation of guineapigs, mice and rabbits resulted in abscesses in the brain from which cultures could in all instances be obtained.

[Other references to cladosporiosis of the central nervous system are: LUCASSE *et al., Bull. Hyg.*, 1955, v. 30, 232; GARCIN *et al., Journées de Mycologie Médical*, 14–15 December, 1956; *La Presse Médicale*, 1949, No. 81, 1201; DEREYMAEKER and DE SOMER, *Acta Neurol. and Psychol. Belg.*, 1955, v. 55, 629.] *C. J. La Touche*

SYMMERS, W. St. C. **Chromoblastomycosis simulating Rhinosporidiosis in a Patient from Ceylon.** *J. Clin. Path.* 1960, July, v. 13, No. 4, 287–90, 2 coloured figs. [19 refs.]

Chromoblastomycosis is usually limited to the cutaneous tissues, but occasionally the mucous membranes have become involved.

The author of this article describes a lesion in the mucous membrane of the nose in a young Sinhalese man who was studying in London during a first visit to England.

According to the patient a small mass had been developing in the left nostril over a period of 2 years and he had first noticed it when he was in Ceylon. More recently, while he was in England, crusting had formed around it. On attempting to remove the crust the patient had caused the mass to bleed. Subsequently there were repeated episodes of haemorrhage from this site.

Detailed examination of the mass revealed a superficial resemblance to lesions found in rhinosporidiosis, and accordingly, it was diagnosed as such. However, histological examination showed that the tissue of which it was composed had the characteristics of a "complex type of chronic granuloma, in which suppurating pseudotubercles were the most characteristic feature, with polymorphonuclear leucocytes, lymphocytes, and a few plasma cells in the loose-textured intervening granulation tissue". Dark golden-brown, rounded bodies measuring about 10 μ in diameter were present singly or in clusters, both in the multinucleated giant cells or lying free in the purulent exudate of the microabscesses. These closely resembled the parasitic phase of *Phialophora pedrosoi*, one of the aetiological agents of chromoblastomycosis.

Although no lesions were present in the skin of this patient the author is satisfied that this was an authentic case of chromoblastomycosis of the mucous membranes, and adds a footnote to the effect that several cases of cutaneous chromoblastomycosis have been recognized in Ceylon since June 1959.

C. J. La Touche

FERNANDEZ BAQUERO, G. & REAUD LESCAY, Berta. Cultivo del *Hormodendrum pedrosoi* del material obtenido por lavado bronquial, en cuatro enfermos de "Cromoblastomicosis". [**Isolation of *Hormodendrum pedrosoi* from Material obtained by Bronchial Lavage in 4 Cases of Chromoblastomycosis**] *Bol. Soc. Cubana de Dermat. y Sifil.* 1960, June–Sept., v. 17, Nos. 2/3, 99–101.

COCKSHOTT, W. P. & RANKIN, A. M. **Medical Treatment of Mycetoma.** *Lancet*. 1960, Nov. 19, 1112–14, 2 figs.

The multiple aetiology of mycetoma has always presented a difficult therapeutic problem; and the fact that most lesions of this disease become, in due course, complicated by secondary infection is well known. Accordingly, drug cover therapy is directed towards a wide range of organisms, often without a fungal agent having been isolated from the lesion or lesions. This approach is often successful in bringing about resolution or partial resolution of at least the grosser features of the disease. Thus surgery may be postponed for a considerable time or indefinitely.

In a group of 18 patients 8 responded well to drug therapy which consisted of the administration of wide-spectrum antibiotics accompanied by oral administration of diaminodiphenylsulphone (dapsone).

The authors describe in this article the clinical course of 3 of their patients who were treated successfully by these drugs. *C. J. La Touche*

RAPAPORT, F. T., LAWRENCE, H. S., MILLAR, J. W., PAPPAGIANIS, D. & SMITH, C. E. **Transfer of Delayed Hypersensitivity to Coccidioidin in Man.** *J. Immunology*. 1960, Apr., v. 84, No. 4, 358–67. [24 refs.]

By various means the authors of this report were able to transfer coccidioidin sensitivity from professional blood donors who were permanent residents in a region endemic for coccidioidomycosis to a number of recipients who did not exhibit sensitivity to undiluted coccidioidin and who did not reside in an endemic region.

In one set of experiments leucocyte extracts obtained from donors' blood and treated with deoxyribonuclease, were injected into the recipient intradermally or subcutaneously at the shoulder, while the challenging dose of coccidioidin (1 : 100) was injected intradermally on the volar aspect of the forearm. In another set of experiments the antigen was introduced at the same site of injection as the leucocyte extract.

It was found that marked local as well as generalized delayed sensitivity could be induced by both these methods, but that with the second method only very minute volumes of leucocytes (0·02 ml.) were necessary to accomplish this.

It was found also that equally good results could be obtained if the leucocyte extract and the coccidioidin dilution were injected as a mixture into the forearm, as was shown when a challenging dose of coccidioidin was injected into the opposite forearm at 6 days following transfer.

Control experiments in which leucocyte extracts were prepared from putatively negative reactors to coccidioidin who had resided in an endemic area produced a negative result in some of the recipients and a positive one in others. On further investigation it was found that all of the donors were more or less sensitive to undiluted coccidioidin.

Finally, a control set of experiments, in which leucocyte extracts were prepared from a negative reactor to undiluted coccidioidin who had never resided in an endemic region, were performed. The results of this last set of

experiments showed that all the recipients except one remained negative to undiluted coccidioidin after transfer.

The duration of transferred sensitivity subsequent to experiment was also investigated, and this was found to vary according to the individual, and was apparently correlated with the initial degree of sensitivity conferred.

C. J. La Touche

RAPAPORT, F. T., LAWRENCE, H. S., MILLAR, J. W., PAPPAGIANIS, D. & SMITH, C. E. **The Immunologic Properties of Coccidioidin as a Skin Test Reagent in Man.** *J. Immunology.* 1960, Apr., v. 84, No. 4, 368–73. [16 refs.]

This report deals with the results of 3 sets of experimental investigations of different groups of people who were subjected to tests with coccidioidin.

The first set of investigations dealt with the "effect on negative reactors of repeated intradermal testing with coccidioidin"; the second with "the anamnestic response of individuals with latent sensitivity to repeated intradermal testing with coccidioidin"; and the third with "the relationship between delayed allergy to coccidioidin, detectable serum antibody, and clinical findings in healthy long-term residents of the San Joaquin Valley".

Results indicate, according to the authors, that the use of graded increasing concentrations of test antigen "could serve to identify weak reactors (who may be missed with a single skin test)", having in mind, of course, the possibility of dual infection, and consequently, cross-reactions with some other deep mycosis.

Results from the second series of tests indicate a response analogous to that found in weak, delayed sensitivity to tuberculin, inasmuch as people who had failed to react to a 1:100 concentration of coccidioidin but reacted to a 1:10 concentration, subsequently reacted to the weaker concentration.

Results from the third series of tests indicate that there was no essential "relationship between the level of cutaneous reactivity to coccidioidin and the presence or titer of complement-fixing serum antibody" in people residing in an endemic area.

C. J. La Touche

PERRY, D. M. & KIRBY, W. M. M. **Acute Disseminated Coccidioidomycosis: Two Cases treated with Amphotericin B.** *Arch. Intern. Med.* 1960, June, v. 105, No. 6, 929–34, 3 figs. [13 refs.]

Amphotericin B, a polyene antifungal drug derived from a species of *Streptomyces,* has been used with increasing frequency for the treatment of systemic mycoses in man.

This article records the results of treating with this drug 2 patients who were suffering from "acute, severe manifestations of disseminated coccidioidomycosis". The response to this form of therapy was, in both cases, most favourable.

The first patient so treated, a Negro aged 29 years, was weak and cachectic

when treatment was started. The dosage, by intravenous injection over a 6-hour period, was gradually increased to 70 mgm. per day. By the 12th day of treatment the blood urea nitrogen had risen to 40 mgm.% ; it was therefore decided to administer the drug in a dosage of 70 mgm. only every other day. As, however, the patient remained acutely ill, prednisone was administered as well in a dosage of 30 mgm. daily by mouth. Following this the patient rallied in a few days, although the blood urea nitrogen " reached a maximum level of 71 mg. % six days after prednisone was started ". After this the blood urea nitrogen fell as did also the temperature. The patient became ambulatory, but exercise caused a recurrence of low back pain, and when an X-ray examination of this area was carried out on 22 September, 1958, much destruction and collapse of the 4th lumbar vertebra was thereby revealed. Consequently, the patient was kept in bed and amphotericin B therapy was continued for another 5 months. When this was stopped the patient was placed in a light body cast in which he remained for 6 months. However, in May 1959, a recurrence of symptoms indicating active coccidioidal infection supervened, and finally, despite a resumption of amphotericin B therapy, the patient died.

Autopsy revealed widespread dissemination of the infection.

The second case was of a 56-year-old Negro who presented with a facial lesion involving the right orbit, nose and mouth. He had first noticed these lesions 6 months before admission to hospital.

He was treated intravenously with amphotericin B in the dosage of 70 mgm. daily for 3 weeks, then 80 mgm. 3 times weekly for 4 weeks, and thereafter, 100 mgm. 3 times a week. Within 7 to 10 days of the initiation of this treatment there was a decrease in soreness of the oral lesions and the patient was able to swallow fluids with less pain. During the 3rd week his appetite improved greatly and he was able to take solid food. Over the next few weeks ulcers on the tongue and other parts of the mouth healed and there was a marked improvement in the lips which had previously been swollen ; other lesions also, including that around the right eye, had completely resolved. The patient experienced a general feeling of wellbeing and his appetite returned. He also put on weight, and continued to do so for 4 months after treatment had been discontinued. It is stated in an addendum that he has had a recurrence of ulcers on the lips and tongue and is being re-treated.

In order to reduce toxic side reactions to a minimum prednisone was administered by mouth in the dosage of 15 mgm. daily, commencing on the 30th day of amphotericin B administration, and also 25 mgm. of hydrocortisone was administered with each intravenous injection of amphotericin B. Administration of steroids concurrently with amphotericin B was considered to be an important factor in combating unfavourable reactions to this drug.

C. J. La Touche

TROPICAL OPHTHALMOLOGY

COLLIER, L. H. **On the Aetiology and Relationship of Trachoma and Inclusion Blennorrhoea.** *Rev. Internat. du Trachome.* 1960, v. 37, No. 4, 585–99, 2 figs. [25 refs.]

The author reviews briefly the work of recent years establishing the aetiological relationship of the elementary-body viruses isolated from trachoma with that disease. He points to the need, however, of large-scale field investigations to correlate the presence of these viruses with clinical signs and the demonstration of inclusions, and he reports some of the findings of such an investigation he is conducting in a Gambian village with a population of 400. Virus isolation proved the more productive investigation since it was obtained from 57·5% of subjects with clinical trachoma stage I and II, whereas inclusions were demonstrated in only 37·5% of them. Considerably fewer people with stage III were positive to either investigation and none was in stage IV. No positive findings were obtained in those with normal eyes or eyes suffering from other conditions. Various bacterial species were isolated; only those belonging to the genus *Haemophilus* appeared to have any correlation with the clinical syndrome trachoma and their role in its pathogenesis has yet to be elucidated.

Turning to inclusion blennorrhoea the author observes that though the relationship of a virus belonging to the psittacosis-lymphogranuloma-venereum group with this condition is established [*Bull. Hyg.*, 1959, v. 34, 1060], differentiation between those strains found in trachoma and those in inclusion blennorrhoea still rests on the differences in clinical picture and epidemiology presented by the two conditions and the result of conjunctival infection of apes with these two agents. Differentiation by serological means—a field of investigation so far largely unexplored—should provide the answer.

S. P. Bedson

FURNESS, G., GRAHAM, Doris, REEVE, P. & COLLIER, L. H. **The Growth of Trachoma and Inclusion Blennorrhoea Viruses in Cell Culture.** *Rev. Internat. du Trachome.* 1960, v. 37, No. 4, 574–84, 3 figs.

A strain of trachoma virus—T'ang—and one of inclusion blennorrhoea—LB1—have been adapted to growth in HeLa cells. The cells were cultivated in Hanks saline containing 10% horse serum, 0·5% lactalbumen hydrolysate, 5% tryptic digest broth and streptomycin 200 μgm./ml.

Attempts to cultivate 2 African strains of trachoma virus in this way were unsuccessful. Little free virus was found in the culture fluid but after 48–72 hours' incubation inclusions in the infected cells were readily observed, both in living unstained preparations examined with the low power of the microscope and in Giemsa-stained preparations. The whole cells, freed by pipetting, were used for passage and 11 serial passages were realized with the T'ang strain and 18 with LB1. Elementary bodies obtained from the infected cells were shown to be infective for the chick embryo yolk sac and to contain the psittacosis-lymphogranuloma-venereum group antigen.

The possibility of using inclusion counts as a method of titration was examined and found to have a standard error of ± 10%.

S. P. Bedson

FURNESS, G., GRAHAM, Doris M. & REEVE, P. **The Titration of Trachoma and Inclusion Blennorrhoea Viruses in Cell Cultures.** *J. General Microbiol.* 1960, Dec., v. 23, No. 3, 613–19.

The cytoplasmic inclusions formed by these viruses are readily seen and identified. And on the not unreasonable assumption that the inclusion-forming unit is a single infective virus particle, a count of inclusions produced in a cell monolayer by a suspension of one or other of these viruses should be a measure of the virus content. Using monolayers of HeLa cells the authors have obtained evidence in support of this contention. The method is shown to be more reliable than titration in the chick-embryo yolk sac. *S. P. Bedson*

JONES, B. R. **Human Inoculations with Trachoma Virus.** *Rev. Internat. du Trachome.* 1960, v. 37, No. 4, 600–608, 7 figs.

With strains of virus isolated from trachoma patients in Gambia, experimental transmission to 4 human volunteers was essayed. The inoculum consisted of a suspension of infected yolk sac. 2 were negative; in one a trachomatous conjunctivitis was produced, but in the 4th typical trachoma with pannus and scarring resulted. The inocula were culturally sterile and secondary bacterial infection did not occur in either of the experimental trachomas. *S. P. Bedson*

INOUE, Y., MURAKAMI, K., OHASHI, T. & ARAKAW, S. **The Clinical Value of Complement Fixation Test (CFT) by the Use of Antigen for Trachoma (TR).** *Rev. Internat. du Trachome.* 1960, v. 37, No. 4, 623–34.

The trachoma antigens used in this work were either 10% saline suspensions of infected mouse brain or 20% saline suspensions of infected chick CAM; they were used untreated. Control antigens were similarly prepared from normal uninfected tissue (apparently anticomplementary at times).

The authors interpret their findings as indicating that the degree of fixation obtained in the test varied directly with the clinical severity of the case and that the sera from those cases which were mild, with a tendency to spontaneous cure or a ready response to antibiotic therapy, gave a negative complement-fixation test. [The presentation of this paper, both as regards English and lay-out, make it hard to follow; it is unconvincing.] *S. P. Bedson*

BIERENT, P., DUPOUX, R. & SCHNEIDER, J. Traitement du trachome par l'acétyl-sulfaméthopyrazine en suspension injectable. Essai en vue du traitement de masse (note préliminaire). [**Preliminary Trials of Acetyl Sulphamethopyrazine in Injectable Suspension in the Treatment of Trachoma**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 210–16.

The authors, while recognizing the value of sulphamethopyrazine in the mass treatment of trachoma, would like to avoid the inconvenience of prolonged weekly or bi-weekly treatment. They started by using an aqueous suspension

of 25% in 10 ml. ampoules each containing 2·5 gm. for intramuscular injection but found that, in a comparable dose, acetyl-sulphamethopyrazine, though slower in action, was more stable and its action more prolonged. They have therefore combined the injection of the acetyl drug with 2 to 6 tablets of 250 mgm. of sulphamethopyrazine orally. The dose is modified according to age and the treatment may be repeated in 3 weeks or more according to the response.

Moderately severe cases clear up in two treatments and light and recent cases after one treatment. Pruritus, florid granulations, pannus and corneal opacities respond to this method; and even symblepharons yield.

This is a preliminary note on the results of comparatively few cases but the authors are encouraged [and well they might be] to persist in this promising line of clinical research in the mass treatment of trachoma. *A. McKie Reid*

See also p. 491, LAGRAULET & TORROELLA [**Study of Ocular Lesions of Onchocerciasis observed in the States of Oaxaca and Chiapas, Mexico**].

TROPICAL ENVIRONMENTAL CONDITIONS

GOLD, J. **Development of Heat Pyrexia.** *J. Amer. Med. Ass.* 1960, July 16, v.173, No. 11, 1175–82, 7 figs. [18 refs.]

This article describes observations made on the development of heat pyrexia in men exposed in the laboratory to dry heat, some for 2 hours at 54·5°C. (130°F.) and others for one hour at 71·1°C. (160°F.) Each subject was removed from the hot chamber when collapse was judged to be imminent. Information was obtained on sweat rate, blood pressure, forearm venous pressure, body heat storage and oxygen consumption, cardiac output and electrocardiographic changes. Other investigations included blood gas analysis, estimations of haematocrit and of plasma osmolarity, and radiographic size of the heart before and after heat exposure. Not all the investigations listed were made on each subject.

During extreme heat exposure there was an increase in cardiac output, forearm venous pressure, and in body heat storage. A quantitative correlation was observed between body heat storage and the rise in forearm venous pressure. Sweating was seen to decline towards the end of each experiment. The diastolic blood pressure fell during heat exposure, but only in young subjects; the size of the cardiac X-ray shadow decreased, and the commonest electrocardiographic abnormalities observed were flattening and ultimate inversion of the T-wave and depression of the S-T segment. There was an average increase of 2·1% in haematocrit, a reduction in the oxygen A-V difference, and an increase in the carbon dioxide A-V difference.

The most important of the conclusions reached by the author are that the primary event in the circulatory collapse of heat pyrexia is high-output cardiac failure and that the cessation of sweating is a result of rising venous pressure.

[This paper has been discussed in a *Lancet* leader (see *Lancet,* 1960, Oct. 15, 856). The conclusions reached by the author offer a possible explanation for mechanisms in heat stroke which have so far escaped understanding. It is right therefore that these conclusions, and the experimental data and discussion on which they are based, be examined carefully and critically in the original before they are accepted or quoted.] *C. S. Leithead*

TROPICAL ULCER

NGU, V. A. **Tropical Ulcers in Ibadan.** *West African Med. J.* 1960, Dec., v. 9 (n.s.), No. 6, 247–55, 6 figs. [12 refs.]

Tropical ulcers are frequent in Ibadan as in other parts of Africa. The author studied 138 patients with tropical ulcers from some thousand attending the hospital. 110 of these were acute ulcers of less than 2 months' duration, with oedematous margin and sloughing base. 28 were chronic ulcers of more than 2 months' duration, with a hard fibrotic border with skin pigmentation.

Age incidence was similar for both acute and chronic ulcers, being highest in the age-group 5 to 15 years.

The site of ulceration was the ankle or lower third of the leg in 81% of the acute, and 86% of the chronic ulcers.

The duration of acute ulcers averaged one month. A week was the minimum period for an ulcer to form fully. Chronic ulcers had lasted from 3 months to 15 years, with an average duration of 2 years.

60% of patients with acute ulcers gave a history of trauma as a predisposing cause, but this was probably an underestimation.

There was no evidence of anaemia, the average haemoglobin concentration of 76% being similar to that of the general population. 11 cases showed sickling. The 12% with positive Kahn reaction was again similar to the general incidence. There was no clinical evidence of malnutrition or of vitamin deficiency.

The bacteriological findings included many organisms, but in 73 of 110 (66%) of the acute cases spirochaetes and fusiform bacilli were found.

Various treatments were used including eusol dressings, eusol with antibiotics, excision and antibiotics, and the use of skin grafts when clean. None of the treatments was completely satisfactory when used in out-patients owing to the failure of patients to continue attendance. The author stresses that admission to hospital may prove the most economical method of treatment in the end.

[There is nothing new in this survey, but it confirms the findings of others in both West and East Africa.] *A. C. E. Cole*

BECQUET, R., GASTEAU, Thérèse & HAPPI, Claude. Étude des rapports entre l'ulcère tropical phagédénique et la drépanocytose au Cameroun. Statistique personnelle concernant le Pays Bamiléké. [**The Correlation between Tropical Ulcer and Sickling in the Cameroons**] *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 160–64.

In the French Cameroons the incidence of tropical ulcer rises from 0·5% in the north to 3 to 6% in the south; and similarly the sickling rate rises from 6·33% to 24%. The authors question whether this is a simple coincidence. They mention humidity as an aetiological factor in ulcer, but do not consider whether it might not also be a determinant of greater malarial transmission, which would induce higher sickling rates. However, they explore the coincidence further by an investigation of 543 Bamiléké. There were 5 ulcer patients among 45 sicklers, and 10 among 498 non-sicklers, a significant difference.

[The abstracter cannot accept the authors' view that sickling is an aetiological factor in tropical ulcer, since it disagrees with the findings of BRAIN in Southern Rhodesia (this *Bulletin*, 1953, v. 50, 241) and of BEET in Northern Rhodesia (*ibid.*, 1947, v. 44, 1091). From the figures of the latter, who examined 2,104 subjects, it can be calculated that the sickling rate was 12·3% and the ulcer rate 8·9%; and that tropical ulcer was slightly *less* common (though not significantly so) in the sicklers.] *Alan B. Raper*

MISCELLANEOUS DISEASES

DAO L., L. Experiencias sobre Enfermedades Tropicales en zonas rurales de Venezuela. [**Studies on Tropical Diseases in Rural Areas of Venezuela**] 393 pp., illustrated. [? 1960.] Roblecito: c/o Mercedes Co., Guarico, Venezuela.

Dr. Dao is Director of the hospital of the Mercedes Company, an oil operating organization in Roblecito in the State of Guarico, Venezuela.

This volume contains a collection of 22 of his papers published between 1939 and 1958 in various medical journals, the references to which are listed. All the papers are in Spanish: in most cases there are summaries in English or French or both, and lists of references. The papers are grouped under 4 headings, namely (1) Chagas's disease, containing 4 papers on epidemiological and clinical aspects, (2) malaria, consisting of 5 papers on clinical and therapeutic features, (3) intestinal parasites, in which the incidence and significance of some of these parasites are discussed in 4 papers, (4) other tropical diseases, and (5) other publications, both of which deal with a miscellany which includes myiasis, vaginal trichomoniasis, tetanus, liver function, a study of pregnant women and other subjects: these two sections account for the remaining 9 papers.

These papers contain much valuable information and original observations: but as most of them were published between 1944 and 1950 and only 4 since

1955, there are no recent data. The collection will, however, prove of considerable value to those who seek information on the subjects discussed, in Venezuela during the periods of observation. *H. J. O'D. Burke-Gaffney*

SACKS, M. I. **Aortic and Coronary Atherosclerosis in the Three Racial Groups in Cape Town.** *Circulation*. New York. 1960, July, v. 22, No. 1, 96–109, 1 fig. [16 refs.]

The three racial groups, white, Cape coloured, and Bantu in South Africa have provided informative material on the incidence of clinical and electrocardiographic evidence of coronary artery disease (VOGELPOEL and SCHRIRE, *Lancet*, 1955, Nov. 26, 1108; and SCHRIRE, *Amer. Heart J.*, 1958, v. 56, 280) [see also this *Bulletin*, 1959, v. 56, 1279]. The present report from the Department of Pathology, University of Cape Town, is concerned with the finding of atherosclerosis in the coronary arteries and aorta removed at post-mortem examination from 1,250 unselected adults who died from natural illness. In 1,180 cases both aorta and coronary vessels were examined, in 53 further cases the coronary arteries only were examined, and in 17 cases only the aorta could be studied. In most cases the vessels were removed, preserved overnight in the refrigerator, and then were graded according to a predetermined classification by the author without knowledge of race, sex or age of the subject.

The results are shown in tables by racial group, age and for each sex separately. These tables should be studied by those interested in the details. Broadly, however, the results are that aortic and coronary atherosclerosis are rare in the Bantu, although severe changes occasionally occur and then affect the same areas of the aorta as in severe cases in whites, that is the abdominal aorta and its bifurcation. In no Bantu case, however, was the marked ulceration and calcification seen which sometimes are seen in the Cape coloured and the white subjects. The differences between the Cape coloured and the white are less marked, but even in groups where coronary atherosclerosis was as commonly encountered in the Cape coloured as in the whites, the former showed a lower frequency of severe luminal narrowing.

There is a discussion of the findings, including reference to the incidence of hypertension, diabetes and myocardial infarction in relation to the findings of atherosclerosis. *S. Bell*

UYS, C. J., VAN DER WALT, J. J., POTGIETER, G. M. & GOLBY, H. H. **A Comparative Study of the Autopsy Incidence, Histological Distribution, and Relation to Cirrhosis, of Liver Siderosis in the Three Racial Groups of Cape Town.** *South African J. Lab. & Clin. Med.* 1960, Mar., v. 6, No. 1, 1–11, 5 figs. [20 refs.]

In view of the difference in opinion over the origin of Bantu siderosis, the authors examined the incidence and degree of deposition of haemosiderin in the livers of Europeans, coloured persons and Bantu in Capetown. Specimens from 1,200 consecutive autopsies were stained with Perl's stain (for visible Fe), with haematoxylin and eosin, van Gieson for collagen, and with Foot's stain for reticulum. Quantitative estimations of iron were not made, but the

degree of siderosis was calculated as follows: Grade A, iron seen in the Kupffer cells or liver cells only; Grade B, seen in both Kupffer cells and liver cells; Grade C, iron in both cells and either free or intracellular in the portal tracts. Siderosis was regarded as becoming the more severe in the order Grade A, B and C.

Siderosis occurred with significantly greatest frequency in the Bantu. Europeans and coloured persons showed about equal incidence. Males were more affected than females and there was no obvious predisposition for siderosis in either form of cell. There was no correlation between siderosis and cirrhosis, but increased portal fibrosis was associated with the higher degrees of siderosis.

The authors conclude that since coloured persons show the same degree of siderosis as Europeans and not a higher degree intermediate between them and the high siderosis observed in the Bantu, dietary habits, including excessive iron intake, are determining factors in siderosis in the latter, rather than malnutrition. *B. G. Maegraith*

Achar, S. T., Raju, V. B. & Sriramachari, S. **Indian Childhood Cirrhosis.** *J. Pediatrics*. St. Louis. 1960, Nov., v. 57, No. 5, 744–58, 11 figs. [24 refs.]

This study which includes the clinical, histo-pathological and epidemiological aspects of juvenile cirrhosis as seen in Madras, India, is based on a series of 310 patients admitted during the period 1950–1958 to the Liver Clinic of the Paediatric Department of the General Hospital, Madras. The series comprised 6 examples of neonatal hepatitis, 4 of congenital biliary atresia, 118 of evident post-hepatitis cirrhosis, 166 examples of persistent, insidious hepatitis and 16 classified as nutritional fibrosis. 40% of the patients therefore appeared to fall into the post-hepatitis cirrhosis group, but in by far the largest group the condition was of indefinite onset and insidious progress. Loss of appetite, low fever, abdominal distension from tympanites and enlarging liver and finally splenomegaly and ascites due to portal hypertension comprised the broad clinical picture. Jaundice was inconstant, mild and transient. Some patients recovered slowly over several years, but those in whom recognizable portal hypertension had developed, deteriorated inexorably to death from hepatocellular failure or from intercurrent infection. No specific aetiological factors could be recognized in the year preceding the illness of this group of children.

The early histological changes in this group of insidious onset comprised multiple foci of liver cell necrosis and an infiltration of inflammatory cells into the sinusoides, but the fibrous tissue reaction was not marked and the stromal architecture was not disturbed. This histopathological picture was common also to many of those whose illness had started with an overt attack of jaundice. In either group, though resolution might occur in a few instances, the liver changes usually progressed to frank cirrhosis resulting in portal hypertension and hypersplenism.

Of the group of insidious onset, 44% are known to have died of hepatic cirrhosis during the 8 years of the study, and 12% were untraceable and were presumed to have died. In 24% the condition appeared to have become arrested, with few or no symptoms. In the post-hepatitis cirrhosis group 46% died and 25% appeared to have reached a stable condition with minimal residual symptoms.

The authors recognized 2 types of sequelae to acute hepatitis. In the first which exhibited vague digestive symptoms and slight, soft enlargement of the liver, histological changes were limited to rare vacuolated liver cells and slight periportal inflammatory infiltration; such livers appeared to be susceptible to further damage. In the second type there were clear signs of liver cell dysfunction, the organ was considerably enlarged and abnormally firm, while the histological changes were those of an actively progressive cirrhosis.

In the late stages, the histopathological picture of the patient who had shown the insidious type of disease was characteristic of post-necrotic cirrhosis. Hyperplastic nodules separated by bands of collagenous connective tissue containing proliferating fibroblasts dominated the scene; fatty infiltration was absent and bile-duct proliferation was rare. Occlusion of the hepatic venous tree was not seen.

More subtle changes were found in very early cases and in some of the apparently normal siblings of such patients. These were common to children whose disease was of insidious or of acute onset. Swelling of liver cells of variable degree was either focal or diffuse, and occasionally acidophilic bodies were seen within or outside the cell wall. Very rarely, accumulations of lipofuscin were seen in the Kupffer cells. A mononuclear cellular infiltration with a few eosinophils were also evident, but the reticular structure was unchanged. During recovery, the vacuolation of the liver cells tended to subside and the inflammatory cellular infiltration to disappear. [The authors point out the similarity of these changes to those seen in early viral hepatitis in adults.]

Among 121 siblings of children showing either the insidious or the post-hepatitis type of liver damage, 50 had hepatomegaly. 22 liver biopsy specimens were obtained from this group, in every one of which pathological changes were demonstrable. During an observation period of 2 years, 13 of those siblings showed clear evidence of a developing cirrhosis.

In a significant proportion—20%—of children suffering from acute hepatitis a similar illness with jaundice had occurred concurrently or previously among adults in the same family. Furthermore, since a highly significant proportion of the siblings of such patients showed histological evidence of occult hepatitis, there was a strong suggestion that the acute hepatitis of adults and children, the disease of insidious onset and early cryptic hepatitis, had a common aetiology. No evidence of ingestion of a hepatotoxic substance could be obtained and the evidence did not suggest a genetic factor; a viral infection is suggested as the most probable aetiological agent.

Another group of 36 children who had initially shown a gross kwashiorkor syndrome with marked fatty infiltration of the liver were observed for as long as 8 years. Mild periportal fibrosis was the only sequel, and cirrhosis did not ensue in a single instance.

Biopsy specimens obtained from 31 infants suffering from congenital syphilis showed a subsiding hepatitis without stromal overgrowth save in a single instance, that of a child of 1 month who died on the day after biopsy. In this case the classical picture of pericellular cirrhosis was seen. The authors suggest that this picture may only occur in overwhelming prenatal infections which result in stillbirth.

[This is an important communication. If one accepts the authors' views, one wonders why juvenile cirrhosis of the pattern seen in Madras is not of ubiquitous distribution throughout the tropical belt.] *J. H. Walters*

STEINER, P. E. **The Etiology of Human Liver Cancer in Africa and the United States of America.** *Trans. & Studies of College of Physicians of Philadelphia.* 1960, Oct., v. 28, No. 2, 61–7. [29 refs.]

The author discusses his findings from a study of 9 representative case collections of liver diseases in Africa, 2 of which included Europeans and one Cape coloured person. He examined the records of some 900 liver cancers, 943 liver cirrhoses and about 1,000 livers of schistosomiasis, malaria, kwashiorkor, epidemic jaundice and other diseases. He compares his findings with published data on liver cancer in America.

The frequency of primary liver cancer, while differing in various parts of Africa, is consistently much higher than in the U.S.A. or in Europeans living in Africa. In places the incidence is greater than all other forms of cancer combined, in others it is more frequent than cirrhosis. In the U.S.A. primary liver cancer supervenes in about 5% of cirrhotic livers, but in Africa about 50% of cirrhotic livers develop primary cancer which also occurs in many non-cirrhotic livers as well. The author thinks there is no reason for considering cirrhosis as a precursor to cancer of that organ.

The disease appears to be essentially the same in both continents, with the hepato-cellular type preponderating. The clinical history is often startlingly short, the tumour large and commencing at an earlier age, but without any increase in childhood. Benign liver tumours are not more frequent in Africa. The typical cirrhosis in African livers is of the post-necrotic type, small and not unusually fatty.

The author could find no support for the idea that liver cancer was associated in Africa with siderosis, malaria, schistosomiasis, alcohol or indigenous brews, or kwashiorkor. No one tribe or ethnic group was particularly susceptible. He did find, however, a geographical correlation between viral hepatitis and liver cancer and suggests that viral hepatitis may be a major factor in the development both of the typical cirrhosis of the liver and primary liver cancer in Africans. One other significant fact was that the three areas of most liver cancer all lay at low altitude.

He concludes: "Knowing now that cancer is more common than cirrhosis in some areas, it becomes reasonable to view both as sometimes caused by the same liver-damaging agent either separately or together". *J. R. Rose*

PARASITOLOGY: GENERAL

RICCI, M. & CRESTA, M. Ricerche sull'accrescimento infantile, in relazione al parassitismo intestinale, nel Comune di Rofrano (Salerno). [**Studies on Infantile Growth in relation to Intestinal Parasitism, in the Municipality of Rofrano (Province of Salerno)**] *Riv. di Parassit.* Rome. 1960, Sept., v. 21, No. 3, 199–216, 12 figs. [12 refs.] English summary.

Rofrano is a depressed town at an arterial cross-roads in Calabria, with 3,176 inhabitants grouped in 576 families. Some 84% of the dwellings have no water

laid on, and 90% lack any sanitation services. Food is consumed in adequate quantities, but it is deficient in protein and in some vitamin and mineral constituents. The rate of growth in the children lags behind the national average.

Only 8 out of 340 schoolchildren examined, in the age-group of 6–12 years, were found without evidence of intestinal parasites. The other 332, or over 97%, harboured one or more species, including *Entamoeba histolytica, Giardia intestinalis, Hymenolepis nana, Ascaris lumbricoides, Enterobius vermicularis* and *Trichuris trichiura*: 117 of the children carried from 4 to 6 species each.

The most heavily infected children were the slowest growing, and this applied more markedly to weight than to height.

The authors selected 100 of the more heavily infected children for experimental treatment and another group of 100 to observe as controls. They treated the former group with Acranil, dithiazanine and piperazine in the Christmas term, and then repeated the piperazine treatment in each of the next 2 terms, thus covering a whole school year. This quarterly treatment, from November to the next June only, failed to keep the children entirely free from parasites and it did not protect them against reinfection. The treated children, however, showed an improved rate of growth, more especially in weight.

[See also this *Bulletin*, 1959, v. 56, 1064.] *J. Cauchi*

Da Costa, O. R. & Cascaes, O. B. Incidência de parasitos intestinais em 100 imigrantes japonêses. [**Incidence of Intestinal Parasites in 100 Japanese Immigrants in the Amazon Region**] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1960, June, v. 11, No. 1, 187–95. English summary (7 lines).

No parasites were found other than those which occur commonly in Brazil.

Clark, T. B. & Wallace, F. G. **A Comparative Study of Kinetoplast Ultrastructure in the Trypanosomatidae.** *J. Protozoology*. Utica. 1960, May, v. 7, No. 2, 115–24, 14 figs. [29 refs.]

The authors have made a comparative study of the kinetoplast and associated structures in cultural forms of *Leishmania tropica, Trypanosoma cruzi, Herpetomonas culicis, H. muscarum, Crithidia fasciculata* and *Trypanosoma lewisi*, as well as in blood forms of the last-named species. These were examined by electron microscopy in thin sections of centrifuged material.

It was found that the kinetoplast of all these flagellates is constructed on the same basic plan: it is an elongated oval structure, surrounded by a membrane and containing bands of dense fibres running antero-posteriorly. In the parasites of vertebrates these fibres occupy the anterior zone of the kinetoplast, while the posterior zone contains less dense fibres or lamellated mitochondrial cristae. In the insect parasites there is no sharp differentiation between the two kinds of fibres.

The axis of the flagellum consists of an axoneme composed of a bundle of 11 fibres; at the base of the flagellum, 9 of these form a cyclinder separated from the axoneme by a basal plate. This cylinder is surrounded by a mass of electron-dense material, representing the basal granule or blepharoplast seen in

stained preparations of trypanosomid flagellates by light microscopy. In view of the different nature of these two structures, the authors restrict the term "blepharoplast" to the cylinder, while the term "basal granule" is retained for the accumulation around it. In discussing the properties of the kinetoplast, the authors arrive at the conclusion that it is mitochondrial in nature.

The most important part of the paper are the numerous micrographs clearly illustrating the appearance of the structures described and their interrelationship.

[See also this *Bulletin*, 1960, v. 57, 455.] *C. A. Hoare*

See also p. 428, GOBLE *et al.*, **Effects of Certain Surface-Active Polyoxyethylene Ethers in Experimental Protozoal Infections.**

ENTOMOLOGY AND INSECTICIDES: GENERAL ZOOLOGY

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

THOMSON, H. M. **A List and Brief Description of the Microsporidia infecting Insects.** *J. Insect Pathol.* New York. 1960, Dec., v. 2, No. 4, 346–85. [Numerous refs.]

BENAIM PINTO, C. Alergia a insectos. Las emanaciones de insectos como agentes etiológicos de rinitis y de asma bronquial. Primeras investigaciones en Venezuela. (Comunicación preliminar.) [**Allergy to Insects. Insect Emanations as Aetiologic Agents of Rhinitis and Bronchial Asthma. First Researches in Venezuela. (Preliminary Report.)** *Acta Med. Venezolana.* 1960, Jan.–Feb.–Mar., v. 8, No. 1, 8–20, 3 figs. [22 refs.] English summary.

The author suggests that dead insect material may be important in the causation of respiratory allergy in tropical countries, and emphasizes (with illustrations) the vast amount of insect life in the air and soil from which disintegrating insect material is derived. Household dust, it seems inferred, contains such debris. Of 80 patients suffering from respiratory allergy, 53 were positive to tests with antigens of a wide range of insects. But, most of these (49 patients) also reacted to other substances, including 41 who reacted to household dust. *D. S. Bertram*

SNODGRASS, R. E. **The Anatomical Life of the Mosquito.** *Smithsonian Misc. Collections.* Wash. 1959, Nov. 4, v. 139, No. 8, pp. iii+87, 30 figs. [Numerous refs.]

Coz, J., Grjebine, A. & Hamon, J. *Anopheles flavicosta* Edwards, 1911 de Madagascar et d'Afrique. [*Anopheles flavicosta* **from Madagascar and from West Africa**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 742–51, 5 figs. [19 refs.]

Wattal, B. L., Kalra, N. L. & Mammen, M. L. **Observations on Certain Morphological Abnormalities in Twenty Species of Indian** *Anopheles*. *Indian J. Malariology*. 1960, Sept., v. 14, No. 3, 291–310, 19 figs. on 11 pls.

Boorman, J. **Studies on the Biting Habits of Six Species of Culicine Mosquitoes in a West African Village.** *West African Med. J.* 1960, Dec., v. 9 (n.s.), No. 6, 235–46, 3 figs. [28 refs.]

The seasonal distribution, biting and activity of several species of culicines (excluding *Aedes aegypti,* to be reported later in this journal) are reported from 24-hour catches on human bait, over a 2-year period, at various sites in the vicinity of Ilobi village 30 miles from Lagos in Nigeria. Catching sites include tree platforms in nearby forest, bush between village and forest, and various places in or near the village frequented by people.

Mansonia (*Mansonioides*) *africana* was by far the predominant species (22,026 specimens), other *Aedes* (*A. grahami, A. simpsoni, A. africanus, A. luteocephalus, A. circumluteolus*) numbering usually a hundred or fewer. Histograms and graphs illustrate the findings and the data for each species are discussed separately at some length in the text, with special regard to its susceptibility to infection with viruses (with literature citations on this) and how its observed habits and activity may contribute to its function as a virus transmitter in nature.

It is thought, in summing the observations, that transmission of viruses in the area from man to man would be by *A. aegypti,* from other mammals to man by *A. africanus, A. luteocephalus, A. circumluteolus* and *A. aegypti,* and between mammals other than man by *M. africana, A. grahami* and *A. africanus.* *D. S. Bertram*

Grenier, P. & Rageau, J. Simulies (Dipt., Simuliidae) de Tahiti. Remarques sur la classification des Simuliidae. [*Simulium* **Species of Tahiti. Observations on the Classification of Simuliids**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 727–42, 3 figs. [13 refs.]

Harvey, T. L. & Brethour, J. R. **Feed Additives for Control of House Fly Larvae in Livestock Feces.** *J. Econom. Entom.* 1960, Oct., v. 53, No. 5, 774–6. [12 refs.]

Several entomologists have tried adding insecticides to livestock diet in order to prevent flies from breeding in the faeces. This paper describes experiments to re-examine the possibility. A boron compound (disodium octoborate tetrahydrate) was found to be effective in preventing house-fly development when

added to cattle manure at 1 gm./kgm. or more. However, when added to the food of steers, up to 100 gm. per head per day, it did not stop fly from breeding in their dung. This contrasts with previously reported success with hens (BURNS *et al.*, *J. Econom. Entom.*, 1959, v. 52, 446). The failure with steers may be due to their excreting most of the boron in their urine, rather than in faeces.

Other tests were made with *Bacillus thuringiensis*, widely used as an insect pathogen, especially for control of caterpillars. A dried spore preparation ($2{\cdot}5 \times 10^{10}$ spores/gm.) was added to cattle faeces and largely suppressed fly breeding at 0·1 gm./kgm. and over. Added to hen feed, at 0·0078 gm. per head per day, it successfully stopped breeding (and completely stopped breeding in faeces from cattle fed 20 gm./head/day).

When added to cattle faeces at 0·2 gm./kgm., its effect on fly breeding was not affected by addition of 0·3 gm./kgm. of aureomycin. (The latter seems to favour fly breeding when added alone.) *J. R. Busvine*

STEGWEE, D. **The Role of Esterase Inhibition in Tetraethylpyrophosphate Poisoning in the Housefly, *Musca domestica* L.** *Canadian J. Biochem. & Physiol.* 1960, Dec., v. 38, No. 12, 1417–30, 2 figs. [30 refs.]

BENJAMINI, E., FEINGOLD, B. F. & KARTMAN, L. **Antigenic Property of the Oral Secretion of Fleas.** [Correspondence.] *Nature*. 1960, Dec. 10, v. 188, 959–60.

The oral secretion of *Ctenocephalides felis felis* was collected in the apparatus described by KARTMAN [this *Bulletin*, 1955, v. 52, 360] in which 1,000 fleas at a time fed through a membrane on distilled water at 37°C. The yield of a lyophilized form of the secretion was about 100 μgm. per 100,000 fleas. Amounts equivalent to the secretion from 3,000 fleas were injected intradermally into guineapigs twice (at a week's interval) and also intraperitoneally, as the secretion in saline alone, or plus an adjuvant. Other guineapigs injected with whole flea abstract, or bitten by 20 fleas, or injected with solutions free of oral secretion, served as controls. Challenges of the variously treated guineapigs were by daily bites of 20 fleas over 5 days a fortnight after the initial sensitization course. Although an antigenic substance inducing sensitization appeared to exist in flea oral secretion, the adjuvant was necessary to elicit its full antigenic properties. *D. S. Bertram*

SHARMA, M. I. D. & SINGH, N. N. **A Note on a Technique for Quantitative Estimation of Susceptibility of Bed-Bugs to Contact Insecticides.** *Indian J. Malariology*. 1960, Sept., v. 14, No. 3, 311–27, 3 graphs. [13 refs.]

The authors list 15 papers dealing with tests of insecticides against bed bugs, giving short notes on the various techniques employed. They do not consider that any of the methods described are entirely satisfactory for assessing susceptibility levels in order to detect insecticide resistance in bugs. They themselves have tried using the WHO test kit intended for determining resistance

in body lice. In this method, the insecticides are applied in powder form to patches of cloth and the insects confined on these for a standard time [WRIGHT and BROWN, this *Bulletin*, 1957, v. 54, 943].

The results obtained gave straight log concentration-probit regression lines for 2 colonies of susceptible bed bugs, DDT, γ BHC or pyrethrins being used. (The slopes were steep with the 2 last mentioned; fair with DDT). These tests were done with a 24-hour exposure time for DDT and $\frac{1}{2}$ or 1 hour with BHC and pyrethrins.

Tests of bugs exposed to papers impregnated with oil solutions [as suggested by BUSVINE, *ibid.*, 1959, v. 56, 990] gave high mortalities in controls after 24 hours' exposure.

It is concluded that the WHO louse resistance test could be adopted for bed bugs. *J. R. Busvine*

LAMONTELLERIE, M. Tiques (Acarina, Ixodoidea) du cercle de Sikasso (République Soudanaise). [**Ticks from the Sikasso Area, Sudan Republic, West Africa**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 751–7. [14 refs.]

COLAS-BELCOUR, J. & RAGEAU, J. Biologie et élevage d'*Ornithodoros capensis* Neumann (Acarien Argasidae). [**Biology and Rearing of** *Ornithodoros capensis*] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 723–7. [16 refs.]

AUDY, J. R., NADCHATRAM, M. & LIM, Boo-Liat. **Malaysian Parasites XLIX. Host Distribution of Malayan Ticks (Ixodoidea).** *Studies from Inst. Med. Res. Federation of Malaya.* 1960, No. 29, 225–46. [24 refs.]

Between 1952 and 1959, 17,683 animals and birds were examined for ticks at the Institute for Medical Research, Kuala Lumpur, Malaya. The findings are reported in this paper. The 25 species of tick are distributed in genera as follows: *Argas pusillus, Ornithodoros batuensis, Ixodes granulatus,* 11 species of *Haemaphysalis,* 2 species of *Rhipicephalus,* including *R. sanguineus, Boophilus microplus,* 8 species of *Amblyomma,* and indeterminate *Dermacentor.* Several are new records for Malaya.

The species and stages of tick, and numbers are then given by tabular methods for various reptiles, birds, bats, other mammals (insectivores, primates including man, carnivores, edentates, rodents, wild pig, mouse-deer, deer, buffalo and domestic cattle). Reptiles were infested only with *Amblyomma* and *Aponomma* species. An as yet unidentified virus was isolated from *Am. cordiferum* from a python. Immature *Amblyomma* and *Dermacentor* occurred on birds and at least 3 species of *Haemaphysalis,* in all stages, also occurred on birds and were exclusively bird parasites. Soft ticks were found on bats. As regards the considerable range of other mammalian hosts, *Am. javanense* was apparently host specific on scaly ant-eater, *R. sanguineus* on dogs, *B. microplus* on deer and cattle. *Ixodes granulatus,* from which Langat virus (TP21) [*Bull Hygiene,* 1957, v. 32, 99] was isolated, was taken on numerous wild rodents at larval and later stages and also as adult ticks. It was, on

occasion, taken attached to man. The commonest ticks on rodents are, however, immature stages of *Dermacentor* and also *Haemaphysalis* and *Amblyomma*. These are also represented in the collections of ticks attached to, besides simply crawling over, man. *D. S. Bertram*

WALTON, G. A. **A Tick infesting the Nostrils of Man.** [Correspondence.] *Nature*. 1960, Dec. 24, v. 188, 1131–2.

The author, whose work on ticks in East Africa is well known to readers of this *Bulletin*, writes from the Department of Zoology, University College, Cork. He relates the experience of 3 experienced entomologists in East Africa who found their nostrils infested with an immature nymph of a tick of the genus *Amblyomma* during visits to primary tropical rain forest in Uganda on occasions in 1952 and 1957. These entomologists were not aware of the ticks crawling over their faces or entering their nostrils. They first noticed a tenderness of the nose when it was touched or blown. There was no irritation or epistaxis and the tenderness disappeared a few hours after the ticks were removed. The lack of reaction to the parasite in man might suggest that nymphs of these ticks normally infest the nasal passages of anthropoid apes: the chimpanzee, *Pan troglodytes* sub. sp., is, in fact, common in these Uganda forests.

Examples of some of these ticks from human nostrils were examined by 3 specialists but were not identified: it was suggested that they might be nymphs of *A. paulopunctatum*, which in its mature stage is a parasite of the giant forest hog in Western Uganda and is distributed in equatorial Africa.

Dr. Walton suggests that persons visiting the Uganda or West African forests could assist in identifying these ticks by examining the nasal passages of mammals, by watching for white ticks falling from the nose of captured chimpanzees or by finding them in their own if they are aware of nasal tenderness. The ticks should be left until they are engorged with blood (about the size of a small pea) when they may become detached and be removed gently with forceps or blown out into a handkerchief. In man they become attached to the nasal septum or upper anterior recess of the anterior nasal chamber.

The ticks should be kept alive in a tin or tube stuffed with moss or moist tissue paper with a piece of rag tied on top and sent for identification to one of the 3 specialists who examined the samples mentioned above, namely:

Dr. Gertrude Theiler, Veterinary Research Laboratory, Onderstepoort, Transvaal, Union of South Africa.

Miss Jane Walker, East African Veterinary Research Organization, Muguga, Kenya.

Dr. Harry Hoogstraal, Department of Medical Zoology, U.S. Naval Medical Research Unit No. 3, Cairo, Egypt. *H. J. O'D. Burke-Gaffney*

RYAN, R. M. Mamiferos colectados en Guatemala en 1954. **[Mammals Collected in Guatemala in 1954]** *Acta Zool. Mexicana*. 1960, June 30, v. 4, Nos. 1/2, 1–19. [12 refs.] English summary.

The collection included a number of rodents and bats, which are described.

COLENO, R. Étude sur les poissons vulnérants et sur les traumatismes causés chez l'homme par les poissons. **[Study of Dangerous Fish and the Injuries Caused by them in Man]** *Méd. Trop.* Marseilles. 1960, Jan.–Feb. & Mar.–Apr., v. 20, Nos. 1 & 2, 7–31 ; 180–208, 7 figs. [160 refs.]

Dangerous fish include those capable of inflicting injury on man actively or passively with or without the complication of envenomation. The organs concerned include teeth, denticles, spines, etc. and the lesions include bites of all degrees of severity, including amputation, cuts, scratches, erosions, stabs and punctures, sometimes penetrating body cavities. In many cases the trauma is associated with the effects of specific toxins secreted by glands and injected *via* special organs. The organs and lesions are briefly defined and the circumstances attending injury are discussed, including the risks of wading, bathing, diving, deep diving, fishing, handling of dead or dying fish, eating fish (for example, the hazard of sharp bones or poisonous flesh) and accidents, including swallowing live fish.

The genera and species of dangerous fish are reviewed and clinical examples of injuries inflicted are described, often in striking detail. The paper closes with a long well-presented list of fish likely to cause injury or intoxication.

The fish concerned are reviewed in zoological order. Sharks are divided into three groups, dangerous, occasionally dangerous, and inoffensive. The first group includes the man-eater, the tiger shark and the blue, cub, hammerhead and the " fresh-water " sharks which infest such rivers as the Hooghly. There is only one genus of sword fish, which grows to as much as 27 feet and is capable of causing severe injuries with its rostrum but not usually with its teeth. Two genera of sting rays are important. Most are found in tropical seas but some go far up the South and Central American rivers. Wounds from rays are serious and sometimes fatal, especially when penetrating to the pleural or peritoneal cavity. Spiney " puffer " fish are described. The depredations of the savage Characidae, which include the dangerous Piranhas of South America are described in detail. This section reads like a cautionary tale for males bathing in the nude. The unpleasant habits of Siluroidides are discussed, including the extraordinary group (Trichomicteridae) which invade the urethra and vagina.

In this catalogue of horrors the Sphyraenidae, which include the barracudas, get surprisingly little space, although the author admits that " a certain number of bites attributed to sharks are probably caused by barracudas ". [On some parts of the African coast this would read like an understatement.] However, other remarkable fish with engaging habits are described, including the Anabas, which can store a reserve of water and exist for some time in the air. This fish should definitely not be held head foremost in the mouth, lest it be swallowed and become anchored in the oesophagus by its backward-pointing spines. A clinical history underlines this warning.

This is a most remarkable and exciting review, containing passages of absorbing interest. The section on sharks is particularly recommended. It contains a fascinating account of the habits of these creatures near the former penal islands of French Guiana in the days when convicts were " buried " at sea, and, among other things, a detailed account of what you must do if attacked by a shark. Concerning the habits of the barracuda, the author says:

" Le Père LABAT (1742) raconte que les bécunes préfèrent les Noirs aux Blancs

et attaquent plutôt un Anglais qu'un Français! Il explique du reste que les Anglais, par suite de leur habitude de manger de la viande, ont une odeur plus forte que les Français, dont la nourriture est plus délicate. Cette odeur exerce une attraction particulière sur les narines des barracudas; ainsi se mêlent les préventions nationales à l'exactitude, ajoute NORMAN qui relate ces faits pittoresque. Maintenant que le beefsteack s'est démocratisé et fait partie de la ration quotidienne des Francais, il serait amusant d'expérimenter à nouveau sur cette question." *B. G. Maegraith*

MISCELLANEOUS PAPERS

NEW YORK ACADEMY OF MEDICINE. **Medicine and Anthropology. Lectures to the Laity, No. 21** [GALDSTON, Iago (M.D.), Editor]. 165 pp., 6 figs. on 3 pls. 1959. New York 11: International Universities Press Inc., 227 West 13 Street, N.Y., U.S.A. [$3.00; 24s.]

This is a series of lectures by different authors, organized by the New York Academy of Medicine under the general heading of Lectures to the Laity, No. 21. The lectures are very good.

There are many sides to this complex subject, and these are brought out convincingly, especially, perhaps, the difficulty of presenting new and strange ideas to people brought up to concepts of disease causation which western scientists think untrue. Essayists who discuss this subject imply that western doctors underestimate the difficulties experienced by people of different cultures in accepting explanations which seem self-evident to us. We do not clearly enough realize that we cannot explain all the phenomena of disease, and that these failures of explanation—which we admit are due to lack of knowledge—are held by our pupils to be serious and perhaps insurmountable obstacles to acceptance of our views. Traditional lore, in which disease is usually attributed to malevolence directed by persons or spirits, can explain everything.

The point is that the disease is not merely due to the parasite, but that the whole ecology of the patient—his physical, mental, social and religious state—is involved, and that in his disease patterns his relationships to his fellow human beings are as important as his relationships to his parasites. Anthropologists are aware of this, though they do not claim to do more than suggest broadly how these ecological factors can best be manipulated in the interests of health. Doctors are not so well instructed, and they should be given more enlightenment on such matters than they receive at present. The drugs they now use are very powerful tools, not only as immediate cures, but as demonstrations of the validity of their conceptions of disease, and in this respect the doctors are in a good position, especially in their relationships with governments. The prospects are therefore good that health is likely to improve

rapidly and extensively in countries hitherto remote from western science, but the improvement would be more sure and more rapid if the experience of the anthropologists, as exemplified in these lectures, was allowed to permeate medical teaching and practice more than it does at present.

The lectures were as follows:—Man, Magic and Medicine, by Paul Fejos; The Humanist looks at the Doctor, by J. W. Dodds; The Ecology of Health, by Marston Bates; Cultural Mentalities and Medical Science, by F. S. C. Northrop; Mental Illness and Acculturation, by A. H. Leighton; Acculturation in Relation to Concepts of Health and Disease, by Raymond Firth.

Charles Wilcocks

REPORTS AND SURVEYS

Colonial Office. **Colonial Research 1959–1960. Colonial Medical Research Committee. Fifteenth Annual Report, 1959–1960** [Himsworth, H. P., Chairman] (pp. 175–232). Cmnd. 1215. 381 pp. 1960. London: H.M. Stationery Office. [17s.]

This will be the last Report of the Committee, which has now been replaced by the recently established Tropical Medical Research Board. Its subcommittees will continue to function as advisory committees of the Medical Research Council.

Review of work in progress

Helminthiasis

(a) *Loiasis in the Cameroons and Nigeria.* Comparative tests on the relative susceptibility of *Chrysops* larvae to residual insecticides indicate that dieldrin is the most efficient agent in these areas. Detailed information has been obtained on the development of larvae of *Loa* in bred *Chrysops silacea* kept at constant temperature. In tests of various possible prophylactic drugs in monkeys and in a few human volunteers, diethylcarbamazine (Banocide) has so far proved the most effective.

(b) *Onchocerciasis.* A two-year follow-up of 10 patients treated with TWSb has shown that the drug has a microfilaricidal effect. In one case microfilariae were still absent after 2 years. In surveys conducted in the Cameroons rain forest all the generally accepted eye lesions were encountered, but they were seldom severe enough to cause blindness.

(c) *Filariasis in East Africa.* Studies have been continued on the vector-parasite relationship in *Wuchereria bancrofti* infection at Kilwa, on the coast of Southern Tanganyika. In view of a report by Chinese workers of a 93·4% immediate cure rate by a single dose of 1 gm. of diethylcarbamazine (Hetrazan), this dose was given to 23 persons with microfilaraemia. Of these, 15 were examined 4 days later; 13 still had microfilaraemia, but the mean microfilarial count showed a marked reduction. All but one of the 15 subjects complained of fever, vomiting and abdominal or joint pains.

(d) *Guineaworm.* Investigations have been continued at Ibadan, Nigeria, on the use of frogs infected with *Camallanus* worms to reduce the incidence of guineaworm in rural areas. This experiment is as yet incomplete. In Western Nigeria observations have been continued on the use of an anti-guineaworm brass sieve by 100 families selected for this trial. Of those who used the sieve only 1·5% developed guineaworm infection, compared with 11% among non-users.

(e) *Schistosomiasis.* At the East African Institute for Medical Research, Mwanza, Tanganyika, a group of 3 scientists are studying the clinical and parasitological aspects of schistosomiasis, snail taxonomy and vector-parasite relationships and snail ecology and molluscicides, in collaboration with another group of workers at Makerere College, Uganda.

In 3 baboons from an area where *Schistosoma haematobium* infection in man is common, no evidence of infection was seen in sections of liver, intestine and bladder.

A new molluscicide, Bayer 73, has given promising results against snails and their eggs in both laboratory and field tests.

A unit based on the Medical Research Laboratory, Nairobi, has been investigating the suppressive effect of monthly injections of antimony dimercaptosuccinate. Early results are described as " not discouraging ".

In England the Unit is studying schistosome physiology and drug action. The reaction of the reticulo-endothelial system to dead and dying flukes is being investigated and work has begun on the phagocytic response to flukes during the time drugs are acting upon them.

Malaria

In East Africa the Pare-Taveta Malaria Scheme has been terminated, save for a small continuing project. Since spraying was discontinued a year ago transmission has remained at a very low level, and such fresh cases as have occurred have been mild. There is as yet no sign that *Anopheles funestus* is re-invading the area.

At Muheza studies have been conducted on the dispersion and activity of *A. gambiae* by the use of radio-isotopes. Of 62,000 insects released 450 were eventually recovered, mostly at a range of a half to one-quarter mile from the point of release. Small numbers of females were caught 21–23 days after release. The mortality in nature among marked mosquitoes was estimated at about 15% daily.

In Trinidad further progress has been made in curbing the incidence of malaria due to *A. bellator* and *A. aquasalis.* A marked fall in malarial incidence has been brought about by the use of antimalarial drugs in prophylaxis and therapy combined with the spraying of houses with residual insecticides and the increased penetration of the spraying of cocoa and forest land with copper sulphate. *Aedes aegypti* has apparently been completely eradicated from Trinidad and Tobago.

In Nigeria experiments in Victoria Island, Lagos, have indicated that a combination of the long lasting but slow acting DDT with the stronger but shorter-lived activity of BHC may hold some promise for breaking the present deadlock in West African malaria eradication.

In the Gambia studies have been continued on the ecology of the *A. gambiae* complex, particularly in respect of movement of adult populations between breeding places and villages.

At the Liverpool School of Tropical Medicine work has been continued on tissue enzymes in malarial infection. Particular attention has been directed to the subject of liver damage in *Plasmodium berghei* infection in mice, and in *P. knowlesi* infection in monkeys, which is less marked but appears to be of the same type.

Virus Diseases

Summaries of researches on this subject carried out in West Africa (Lagos), East Africa (Entebbe), Trinidad (Port of Spain), the Gambia (Fajara) and the United Kingdom (London School of Hygiene and Tropical Medicine) occupy 13 pages of the Report. It is impossible to do justice to this mass of material in an abstract such as this, but the work on yellow fever in West Africa, on mosquito ecology in East Africa, on Venezuelan equine encephalitis in Trinidad, trachoma research in the Gambia and the fractionation of arborvirus by chromatography at the London School of Hygiene and Tropical Medicine are items of particular interest.

Physiological and Nutritional Research

Studies on body composition have been continued at the East African Institute for Medical Research, Mwanza. Serum protein studies, including determination of the urinary excretion of iron by African children exposed to malaria, were carried out in collaboration with the National Institute for Medical Research, London, where parallel examinations of the children's blood serum for haptoglobins were undertaken. The concentration of iron in the urines was very small.

Analysis of samples of milk and blood serum from African nursing mothers in an area where there was considerable food shortage yielded results similar to those obtained from a group of reputedly malnourished Ghanaian lactating women previously analysed.

Surveys of nutritional and eye diseases have been carried out in the vicinity of Lake Victoria and in the Central Province of Tanganyika. Vitamin A deficiency was the outstanding problem in Central Province, but was not encountered near Mwanza. Marked abnormalities of refraction consisting of a high incidence of axial ametropia, mixed astigmatism, anisometropia and a wide scatter of the aberrations of emmetropia were also found in children in Central Province.

At Mulago Hospital, Kampala, the MRC Infantile Malnutrition Research Unit has concentrated on the development of a biscuit meal made from whole groundnuts, maize flour, cane sugar, cotton-seed oil and dried skim milk which has yielded very promising results, and biochemical changes caused by malnutrition in the tissues of young children. Research has also been carried out on a number of problems relating to the pathology of kwashiorkor.

In Jamaica the Tropical Malnutrition Unit of the MRC has undertaken a number of investigations on protein malnutrition in infants. These are summarized under the headings " Nitrogen metabolism and requirements ", " Basal metabolic rate ", " Protein synthesis and breakdown ", " Magnesium deficiency ", " Enzyme changes ", " Phospholipids in tissues and blood ", " Folic acid metabolism ", " Composition of milks " and " Studies on an Idiopathic Paraplegic Syndrome in adults ". Recent evidence suggests that this syndrome may be an atypical late manifestation of treponematosis, possibly non-venereal.

In the U.K. work on experimental protein malnutrition in young pigs has been continued at the Human Nutrition Research Unit of the MRC, London, and it is hoped to apply the resulting data to problems of nutrition in human subjects. At the London School of Hygiene and Tropical Medicine work has continued on the protein value of tropical foods and dietaries. A grant provided by the Rockefeller Foundation will be used to finance an enquiry into Jamaican foods and diets. It has recently been established that hypoglycin, a substance obtained from the ackee fruit of Jamaica, is an antimetabolite of riboflavine.

Investigations on sickle-cell trait and sickle-cell anaemia have been continued by workers in the field and in laboratories in Britain. Intensive studies have been undertaken on the various types of haemoglobin at these centres. A new haemoglobin variant has been described in a Turkish Cypriot woman and an abnormally unstable haemoglobin fraction was encountered in 3 cases of erythro-leukaemia in middle-aged subjects. Methods for the separation of human haemoglobin species with particular reference to the normal adult and foetal forms and the minor components have also been studied.

At St. Bartholomew's Hospital the study of the abnormal foetal haemoglobin ("Haemoglobin Bart's") has been continued and this has proved to be without alpha chains. A basic abnormality appears to exist, consisting of a deficiency of alpha chains, which can give rise to Haemoglobin H as far as adult haemoglobin is concerned, and to Haemoglobin Bart's as far as foetal haemoglobin is concerned. Studies on material from the Congo have clarified considerably the understanding of the inheritance of haemoglobins. It is now accepted that some abnormal haemoglobins have their mutational change in the alpha chain and some in the beta chain.

In a study of the effect of magnesium on thrombin generation time, 2 children with sickle-cell anaemia were treated with magnesium. This had no effect on the haemoglobin level. The study continues, in the hope of finding a preventive treatment for infarctive sickle-cell crises.

Leprosy

In Northern Nigeria studies have been conducted by the Oxford Leprosy Research group. Changes in the structure of skin and nerves were investigated in various types of leprosy following treatment with Etisul ointment. In lepromatous cases very marked reduction in the number of bacilli in the dermis was observed after 3 weeks' treatment, but acid-fast bacilli could still be found in peripheral nerves in the same biopsy. In Katsina Province 791 children were selected for lepromin and tuberculin skin testing. Also 278 tuberculin negative children were vaccinated with lyophilized vole bacillus vaccine irrespective of their lepromin responses. Lepromatous material was collected for cultivation studies and for the manufacture of lepromin at Oxford.

In Alupe, Kenya, signs of resistance have been noted in patients on DPT (diphenyl thiourea, Ciba 1906) who have completed 3 years of treatment, followed by the appearance of new lesions and an increase of bacilli in lepromatous patients.

Good results have been obtained with Etisul, but it appears that all the benefit from this drug is obtained in the first few months. Improvement is permanent and maintained if DDS is used as the accompanying and following

drug. It is considered that Etisul is safe for general out-patient use, provided adequate administrative control is feasible.

Pharmacological studies have been made on DPT and similar work on di-dimethyl-amino-diphenyl thiourea, DDS and diamino-diphenyl sulphoxide is in progress.

At Makerere College, Uganda, radioactive tracers are now being used as a method of detecting biochemical changes in *Mycobacterium leprae* when subjected to the action of sulphones.

In the U.K. studies on the morphology of leprosy bacilli have been continued at the National Institute for Medical Research. Further work has been done on the multiplication of *Myco. lepraemurium* in cell cultures and attempts to transmit *Myco. leprae* to experimental animals have been vigorously pursued and extended.

An expedition from the Strangeways Laboratory, Cambridge, to Uganda and the Congo resulted in the collection of biopsy material from a number of leprosy cases of different types, treated and untreated, which is now the subject of intensive study.

Tuberculosis

In East Africa therapeutic trials of companion drugs for isoniazid as alternatives to PAS and streptomycin have continued, with the object of finding a cheap, effective and easily administered regimen suitable for routine chemotherapy, under sub-optimal conditions of supervision.

For severe, extensive disease in Africans, isoniazid alone in low dosage is inadequate. Isoniazid plus PAS was found more effective than isoniazid alone.

Comparative trials of isoniazid in combination with thiacetazone, DPT or PAS showed that the isoniazid/thiacetazone combination was almost as satisfactory as the isoniazid/PAS. DPT was found to be ineffective as a companion drug for isoniazid and was not further studied after the first six months.

It is noted that the increase in isoniazid resistance observed in the last 3 years tends to impair the usefulness of this drug for routine therapy.

In Ghana an investigation of methods of applying BCG vaccination has begun. Some 5,000 vaccinations were to be completed early in 1960 and conversion rates were due to be estimated after 4 and 12 months.

Reference is also made in the Report to work in the Gambia on anaemia and hookworm infection in a village following virtual elimination of malaria, which is as yet incomplete, and to an investigation to determine the efficacy of diethylcarbamazine in *Wuchereria bancrofti* infection. The latter study indicates the feasibility of field control of *W. bancrofti* infections in West Africa by mass treatment of populations at intervals of 3–4 years.

A number of entomological studies have been undertaken in the Gambia in collaboration with Dr. D. J. Lewis of the British Museum, London, who has also made extensive studies on Simuliidae and Phlebotominae in Kenya and the Southern Cameroons.

Other research activities referred to in the Report include investigations on the toxicity of bush-teas and epidemiological research in Jamaica, field trial of antityphoid vaccines in British Guiana, research on leishmaniasis in British Honduras, and a number of miscellaneous projects aided by relatively small research grants. *G. Covell*

CENTRAL OFFICE OF INFORMATION. **Reference Pamphlet No. 12. 2nd Edition. Health in the United Kingdom Dependencies.** 37 pp., 16 figs. on 8 pls. [Refs. in footnotes.] 1960. London: H.M. Stationery Office. [4s.]

The object of this pamphlet is to set down the improvements of medical services and health that have been achieved in the United Kingdom dependencies, mainly but not exclusively since the war. There are articles on malaria, leprosy, trypanosomiasis, yellow fever, yaws, venereal diseases, tuberculosis, blindness, hookworm and poliomyelitis, a summary of policies on the preventive aspects of medicine, and a brief history of research into problems of human nutrition, and of efforts to tackle them. The many organizations concerned with health in the United Kingdom dependencies are detailed and described. Apart from the Colonial Office itself, those mentioned include the London, Edinburgh and Liverpool Schools of Tropical Medicine, the Bureau of Hygiene and Tropical Diseases, the World Health Organization, and several voluntary bodies. Training methods and policies also are detailed in this section, which is full of useful information. Finally 5 tables are given: expansion of health facilities 1950–1958 (in 12 dependencies); deaths due to parasitic or infective diseases 1947–1957 (in 4 dependencies) divided into "malaria" and "other"; decline in crude death rates over 25 years, 1930–1955 (in 12 dependencies); infant mortality rates 1935–1958 (in 10 dependencies); expectation of life in varying post-war years (in 9 dependencies).

The pamphlet is well written, accurate and comprehensive, and is presented with a persuasive modesty. Having been prepared for popular consumption, references to the sources of information are not given. They would have been of value to the serious student, but even without them this is a useful and praiseworthy publication.

[For review of the first edition, see this *Bulletin*, 1956, v. 53, 1192.]

B. B. Waddy

BOOK REVIEWS

MANSON'S TROPICAL DISEASES. **A Manual of the Diseases of Warm Climates.** Edited by Sir Philip H. MANSON-BAHR, C.M.G., D.S.O., M.A., M.D., D.T.M. & H., F.R.C.P. 15th Edition. pp. xiv+1177, numerous illustrations. 1960. London: Cassell & Co. Ltd., 35, Red Lion Square, W.C.1. [84s.]

All who have awaited with increasing anticipation the XVth edition of this scholastic cornucopia will find that their patience is amply rewarded. Six years is a long interval between editions of a standard textbook, and Sir Philip Manson-Bahr has grasped the opportunity afforded by recent progress in tropical medicine to rewrite older chapters and to incorporate much new material.

The work begins with an account of the preparation for tropical residence, emphasizing the value of prophylactic inoculations against infectious disease, among which poliomyelitis vaccination might well have been included.

A new chapter on tropical anaemias begins realistically with iron-deficiency states, and the haemoglobinopathies are dealt with at greater length than in the XIVth edition.

The chapter on malaria shows evidence of compression although quinine is still dealt with *in extenso*, a whole page being given to the details of its intramuscular administration. The therapy of this disease is made easier to comprehend by a new summary of drug treatment.

In the account of sleeping sickness, notable advances in epidemiology and treatment are fully described, although stilbamidine, which has little to recommend it, is still mentioned. The clinical aspects of leishmaniasis have been rewritten, and include an illustrated account of chiclero's ulcer.

Among the typhus group of fevers, trench fever now receives only passing mention while new geographical types of tick typhus are described. The account of Q fever has been extended: it is still included among the typhus group but it would seem more appropriate to use the term "rickettsial diseases".

Noteworthy in the revised section on plague is the account of rodenticides. At the end of this chapter comes an essay on the subject of zoonoses, with a glossary of the scientific terms used in this comparatively new field.

The section on virus diseases contains much that is new, including the recent epidemiology of yellow fever in Central America and the prevention of rabies by hyperimmune serum. The ever-important subject of smallpox is emphasized by an admirable two-page summary. Sir Philip is less at home with the more recently discovered arthropod-borne viruses, which seem to the reviewer worthy of more space and the mention of Casals's classification. In obedience to aetiological considerations, Kyansur [*sic*] Forest disease appears in isolation as a sub-section of Russian spring-summer encephalitis.

The chapter on heat hyperpyrexia has been extended; this difficult subject is treated with remarkable clarity.

Important modifications have been made to the accounts of intestinal diseases, especially in the sections on treatment. Normal saline transfusions are recommended for cholera, Rogers' modification having been omitted. It is interesting to note that the role of antibiotics in the treatment of amoebiasis is less emphasized than in the preceding edition. Much of the chapter on sprue has been rewritten, and now includes an account of investigations by jejeunal biopsy.

The chapter on leprosy is entirely new, and includes detailed accounts of reactional states and new additions to the therapeutic armamentarium.

On the aetiology of yaws, the author still defies the persuasive arguments of the unitarians, although Hudson's case is stated fairly enough. In this chapter the habit of dealing with curative drugs in more or less historical order is misleading. The first paragraph (p. 579) states "The most generally used drug at the present time is neosalvarsan". It is not immediately clear that this startling remark refers to the choice of arsenical compounds only. No longer, however, are oral arsenicals recommended, and a thorough account of the use of penicillin follows in due course.

In rewriting the account of mycetoma the author has drawn upon the fine recent work of Abbott. The subject is treated exhaustively although the aetiological arrangement is not helpful to clear understanding. It is a little disappointing, too, to read "The only effective treatment is amputation . . .".

Accounts of systemic fungus diseases, particularly histoplasmosis, have been amplified with great lucidity.

The chapter on encephalitides includes much new matter and an extended account of poliomyelitis.

Cat-scratch disease is given two or three hundred new words, somewhat incongruously included under "Tropical Venereal Diseases". Craw-craw has commendably been eliminated as a skin disease in its own right, being mentioned only as a synonym of scabies. Griseofulvin is given as curative in tinea imbricata, and an interesting account of urticating and vesicating insects is provided.

The important controversial subject of tropical eosinophilia is now described as a manifestation of visceral larva migrans. The new passage on visceral larva migrans due to *Toxocara* larvae would be better placed as a sequel to this account rather than under "Myiasis".

The important helminthiases have been revised, particularly with regard to their treatment. Emetine has been discarded for schistosomiasis, and santonin for ascariasis, and in their place come newer names such as TWSb, piperazine and, for ankylostomiasis, bephenium, which promise to familiarize themselves even more with the passage of time.

Other newly-introduced subjects include veno-occlusive disease and sea-snake poisoning.

The well-known appendices on Medical Zoology are retained. The section on toxoplasmosis has been revised and made more legible to the naked eye, and would easily have graced one of the clinical chapters. No one has ever doubted the value of these appendices, although the author willingly exposes himself to the risks inherent in zoological nomenclature.

Incidentally, *Bulimus tentaculata* [*sic* in the text, though correctly shown as *tentaculatus* in the index] is not a host of *Opisthorchis felineus*.

The book as a whole will remain famous for the charm and detail of its clinical descriptions. The diagnosis of hepatic amoebiasis, the classical account of filariasis, the sheer entertainment of koro, still sparkle with humanity. These and other passages from the former edition, together with much that is new, are written in the grand style, known and admired the world over as "Manson-Bahroque". Where controversy is thrust aside in passages such as "All that the great majority of mild paratyphoid cases require is a soap-and-water enema every other day . . ." and "In the vast majority of [*S. haematobium*] cases the patient experiences no trouble whatever", one realizes that this is a book for the connoisseur rather than for the beginner. As a gesture of defiance to the advocates of the metric system the dose of vitamin B12 is given as "1/3240 gr. in 15 min.", but only an uncompromising reader will overlook the implied message that the substance is one of the most potent known to medicine.

In rising to the occasion, Sir Philip has outstripped his renowned publishers. Among hundreds of thousands of closely-knit words, typographical errors are, perhaps, unavoidable; but "tounges" and "amoebias" in block capitals are less easy to forgive. Some of the plates are ill-situated in relation to the text and even to their legends, and the map which displays Abyssinia, the Gold Coast, and the Anglo-Egyptian Sudan inevitably carries an old-fashioned look in this political age.

The edition is very well illustrated with dozens of new clinical photographs;

the accommodation of 459 figures has, of course, demanded much compression of the text, and the profusion of small type considerably reduces the pleasure of reading. This seems unavoidable; as it is, the volume weighs nearly four pounds, which suggests that its sub-title of "A Manual . . ." will appeal only to readers with unusually large hands.

Criticisms notwithstanding, the reviewer, who has sat many times at the feet of Sir Philip Manson-Bahr, is humbled by the magisterial flow of this tremendous compilation. *A. J. Duggan*

ADAMS, A. R. D. & MAEGRAITH, B. G. **Clinical Tropical Diseases.** 2nd Edition. pp. x + 540, 72 figs. 1960. Oxford: Blackwell Scientific Publications Ltd., 24–25 Broad Street. [52s. 6d.]

ERRATUM

In his criticism of the chapter on snake bite [this *Bulletin*, 1960, v. 57, 1233–5] the reviewer incorrectly stated that Elapidae and Hydrophiidae belong to the family Colubridae.

A classification of the snakes mentioned, which is generally accepted at present, is:—

Family: Colubridae
including
sub-family Colubrinae—fangless snakes (Aglypha)
sub-family Boiginae—posterior grooved fangs (Opisthoglypha)
Family: Elapidae (or Micruridae)—anterior grooved fangs (Proteroglypha)
Family: Hydrophidae—anterior grooved fangs (Proteroglypha)
Family: Viperidae—tubular fangs (Solenoglypha)
sub-family Viperinae
sub-family Crotalinae [or Family: Crotalidae]

A full classification of snakes will be found in "Reptiles of the World" by Raymond L. Ditmars, 1933.

PRYWES, Moshe [Edited by]. **Medical and Biological Research in Israel.** pp. xix+562, illustrated. 1960. Jerusalem: The Hebrew University. U.S.A.: Hadassah, The Women's Zionist Organization of America.

When a people achieves autonomy there is often a great outburst of development designed to increase prestige. In Israel self-determination was followed in many different fields by great advances which were based on the sound foundation of research and practice built up over the previous 40 years. This book is an appreciation of what has been accomplished during the 10 years following the founding of the state of Israel in 1948, and it provides an assessment of what still remains to be done. The problems which had to be solved were serious and numerous, and sometimes unusual. The country, though small, contains three different climatic zones with corresponding flora and fauna, and, being situated at the junction of two great land masses, it is liable to epidemic and epizootic spread of disease from both. Moreover, immigrants have come from all parts of the world, bringing with them the diseases of the countries of their birth.

The book is divided into three parts. The first is introductory and short. It describes in three chapters the history and scientific background in Israel, the various scientific institutions and their activities, and the facilities for medical and biological education. It is astonishing to note the large number of high-grade research institutions and the high doctor: patient ratio of 1: 400.

Part II is a record of achievement in regional and applied research. The influx within 10 years of almost a million people into a small country of which only 20% is arable land and a further 15% suitable for pasture or afforestation, necessitated a rapid and vast expansion of production of staple requirements, which could only take place after elimination of many limiting factors. Important health problems resulted from the introduction from the tropics and subtropics of large numbers of immigrants with low sanitary standards who had to be adapted to a European country and mode of life, and the population had to be protected against diseases thus introduced from outside. Applied research is covered in 4 sections, each consisting of a number of chapters devoted to specific subjects. Space does not permit a list of the wide range of subjects covered, but many of them are of great interest. Included are accounts of the organization of Israel's health services, based on the community and family health centres, and of their system of health insurance.

The third part consists of 5 sections dealing respectively with experimental biology, experimental and clinical medical research, botany, zoology and a brief section on the history of biology and medicine in Israel. The sections are subdivided into a number of sub-sections, 30 in all, concerned with specific fields of research. These are written for the expert, and medical readers will be interested especially in the sections on clinical research and on individual organs.

This is a record of astonishing industry and success. In spite of adverse conditions factors limiting productivity were reduced or eliminated so that production rapidly equalled or bettered that in other parts of the world. These practical results were made possible only by intensive fundamental research. References given in the text number some 2,000, many of them in journals or books not readily accessible to the ordinary scientist. Every biologist who consults this volume will find in it sections which will interest him. It is not a book to read systematically, but to dip into for interest or to refer to a specific subject. A copy should be available in all medical or biological libraries.

T. H. Davey

NOTICE

A Conference will be held by the SOCIETE DE PATHOLOGIE EXOTIQUE on 16 and 17 May 1961, on **Amoebiasis.**

Full details of the programme may be obtained from:

Le Secrétariat de la Societe de Pathologie Exotique,
à L'Institut Pasteur,
25 Rue du Docteur Roux,
PARIS XV°.

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